

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
5 June 2003 (05.06.2003)

PCT

(10) International Publication Number  
WO 03/045557 A2

- (51) International Patent Classification<sup>7</sup>: B01L 3/00, G01N 27/447, B81B 1/00
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- (21) International Application Number: PCT/GB02/05367
- (22) International Filing Date: 27 November 2002 (27.11.2002)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 0128350.6 27 November 2001 (27.11.2001) GB
- (81) Designated States (*national*): AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK (utility model), SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
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- Published: — without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 03/045557 A2

(54) Title: APPARATUS AND METHODS FOR MICROFLUIDIC APPLICATIONS

(57) Abstract: Non-rigid tape apparatus and fabrication methods for microfluidic processing applications such as gel electrophoresis are provided, where microfluidic processing is performed on selected areas. Parts of the tape are formed by high pressure plastic film forming. Membranes and other structures are self sealing during and after penetration by pipettes and electrical probes. Rigid exoskeleton elements protect the non-rigid parts during processing and facilitate transport of the tape.

1 Apparatus and Methods for Microfluidic Applications

2

3 This invention relates to fabrication and processing  
4 technology for microfluidic applications in chemical and  
5 biological processing and analysis, in particular  
6 fabrication and application of non-rigid apparatuses  
7 optionally in the form of a tape.

8

9 In the field known as "lab-on-a-chip", electronic,  
10 microfluidic and bio processes are combined at chip scale  
11 to bring dramatic productivity and cost benefits to  
12 fields as diverse as high throughput screening, bio-  
13 molecular assays and point of care diagnostics.

14

15 Fabrication technologies are known that have been  
16 developed in the microelectronics industry and then  
17 applied to biotechnology and biomedical industries.  
18 However, compared to electronic based devices,  
19 biotechnology devices are much more diverse in order to  
20 enable the manipulation of a large variety of bio  
21 materials, fluids and chemicals. Improvements in  
22 performance, throughput and cost have been achieved by  
23 reducing the size and volume in miniaturised biosystems.

1

2 These "Lab-on-a-chip" solutions have increased the amount  
3 of functionality per apparatus by miniaturisation. The  
4 problem with increased miniaturisation is the complexity  
5 of smaller scale processing and the large cost of  
6 equipment for microfabrication. Furthermore,  
7 conventional lithographic and etching processes adopted  
8 from the microelectronics industry require rigid  
9 apparatuses.

10

11 Glass apparatuses for microfluidic applications are  
12 known, such as the LabCHIP from Caliper Technologies Corp  
13 (Mountain View, CA), US Patent 6,274,089. The glass  
14 apparatus is attached to a plastic moulded cartridge  
15 which incorporates wells for loading test samples,  
16 reagents and gel.

17

18 Rigid plastic apparatuses are known, such as the LabCard  
19 from Aclara Biosciences Inc (Mountain View, CA), US  
20 Patent 6,103,199. A tooling process involving patterning  
21 and electroplating is used to create embossed  
22 microchannels on the card surface.

23

24 "Lab-on-a-CD" devices such as from Gamera and Gyros use  
25 centrifugal force of a rotating disk as the microfluidic  
26 pumping mechanism, e.g., Gamera Bioscience Corporation  
27 (Medford, MA), US Patent 6,063,589.

28

29 The above are all discrete devices which require further  
30 handling steps for continuous operation. They are also  
31 inefficient for single test operation.

32 Silicon apparatuses are known, such as the Nanogen chip,  
33 which is a microfluidic microarray device, where the

1 microarray is selectively doped with biological or  
2 chemical probes which can be polarised electrically to  
3 attract or repel molecules from the sample material under  
4 test.

5  
6  
7 For example, US Patent 5,858,195 to Lockheed Martin  
8 Energy Research Corporation (Oak Ridge, TN) describes a  
9 microchip laboratory system and method to provide fluid  
10 manipulations. The microchip is fabricated using  
11 standard photolithographic procedures and etching,  
12 incorporating an apparatus and rigid cover plate joined  
13 using die bonding. Capillary electrophoresis and  
14 electrochromatography are performed in channels formed in  
15 the apparatus. Analytes are loaded into a four-way  
16 intersection of channels by electrokinetically pumping  
17 the analyte through the intersection.

18  
19 These approaches require time consuming additional steps  
20 of picking and placing discrete apparatuses which  
21 increases the overall processing cycle time in  
22 microfluidic applications.

23  
24 "MicroTape™ - A 384 Well Ultra High Throughput Screening  
25 System" Journal of the Association for Laboratory  
26 Automation, May 1999: Volume 4, Number 2, p. 31, Astle,  
27 T.W., teaches of a tape device designed for storage of  
28 liquid compounds in smaller volumes (typically 10 ul)  
29 than the industry standard 96 or 384 well micro-titer  
30 plate (MTP). Tape storage is in a pattern identical to a  
31 384 well MTP. In effect, MicroTape™ is an alternative  
32 passive storage medium to the micro-titer plate.

33

1 The primary features of MicroTape™ are:

- 2 1) bulk compounds typically stored in 96 or 384 well  
3 micro-titer plates can be transferred into a smaller  
4 volume storage medium, i.e. the MicroTape™, and then  
5 stored within the medium for future use at low  
6 temperature. When this array of compounds is required for  
7 test, only one section of tape (i.e. a 384 well section)  
8 need be retrieved and defrosted, rather than the whole of  
9 the bulk compound medium.
- 10 2) the MicroTape™ incorporates a separate sealing  
11 membrane to protect the compound during storage. This  
12 membrane is capable of being de-sealed and re-sealed.
- 13 3) use of MicroTape™ for Polymerase Chain Reaction (PCR)  
14 processing. The concept takes a reel/roll of MicroTape™  
15 and uses alternate immersion in hot and cold water tanks  
16 to perform thermal cycling for the PCR process.

17

18 The limitations of this approach are:

19

- 20 - It's well capacity is 10ul which is much larger scale  
21 than lab-on-a-chip.
- 22 - It is not patterned microfluidic channels.
- 23 - It is not analytical, i.e. does not incorporate gels or  
24 analytes through which molecular separation or  
25 purification can be accomplished.
- 26 - It is not electrically active, i.e. incorporating  
27 electrical elements or interfacing with electrical  
28 elements i.e. it is simply a carrier.
- 29 - The PCR processing is performed on the whole reel  
30 rather than on selectable areas or segments of the  
31 tape.

32

1 In the contemporary art of gel electrophoresis, including  
2 the emerging field of miniaturised systems, a common  
3 means of detection is to capture an image of these layers  
4 using electro-optical means. A convenient method is to  
5 use a 2 dimensional CCD (Charged Coupled Device) detector  
6 array (an area array) to capture the appearance of the  
7 permeation layer area in a single "snapshot" image.  
8 Another convenient method is to use a 1 dimensional CCD  
9 array (a line array) and move it relative to the  
10 permeation layer such that the full image is built up  
11 from many adjacent line images.

12

13 It would be advantageous to provide an apparatus for  
14 microfluidic applications that allowed an increased area  
15 for microfluidic processing, without requiring an  
16 increase in miniaturisation and the associated complexity  
17 of processing.

18

19 It would be further advantageous to provide an apparatus  
20 for microfluidic applications that facilitated loading  
21 and transport of analytes and reagents both during and  
22 after apparatus fabrication.

23

24 It would be further advantageous to provide an apparatus  
25 that allowed continuous processing of a moving apparatus.

26

27 It would be further advantageous to provide an apparatus  
28 that allowed a variable area on one apparatus, while  
29 using a fixed size of apparatus handling mechanism.

30

31

1 It would further be advantageous to integrate information  
2 storage and management systems within or on the apparatus  
3 for use with simple detection methods.

4

5 It is an object of at least one aspect of the present  
6 invention to provide an apparatus for microfluidic  
7 applications.

8

9 It is a further object of at least one aspect of the  
10 present invention to allow an increased area for  
11 microfluidic processing and novel dynamic processing  
12 steps both within and of the apparatus, while using  
13 simple fabrication processes and apparatus handling  
14 techniques.

15

16 In this document, a probe is defined as including  
17 mechanical probes, electrical probes and pipettes for  
18 fluidic manipulation.

19

20 In this document, indexing patterns are defined as  
21 including patterns for facilitation mechanical movement,  
22 detection of position, detection of movement, and display  
23 and recording of information.

24

25 In this document, mass transport is defined as transport  
26 of mass relative to the apparatus.

27

28 According to a first aspect of the present invention,  
29 there is provided an apparatus for microfluidic  
30 processing applications, wherein said microfluidic  
31 processing is performed on a selected area of a plurality  
32 of areas each individually selectable on said apparatus,  
33 characterised in that the apparatus is non-rigid.

1  
2 According to a second aspect of the present invention,  
3 there is provided an apparatus for mass transport  
4 microfluidic processing applications, characterised in  
5 that the apparatus is non-rigid.

6  
7 According to a third aspect of the present invention,  
8 there is provided an apparatus for microfluidic  
9 processing applications, characterised in that the  
10 apparatus comprises at least one rigid member and at  
11 least one non-rigid member.

12  
13 Preferably the apparatus comprises at least two non-rigid  
14 members.

15  
16 Preferably said non-rigid member is a tape.

17  
18 Preferably there are a plurality of rigid members each  
19 associated with one of a plurality of areas each  
20 individually selectable on said apparatus.

21  
22 Preferably said rigid member comprises access ports.

23  
24 According to a fourth aspect of the present invention,  
25 there is provided a method of fabrication of an apparatus  
26 for microfluidic processing applications, comprising the  
27 step of attaching at least one rigid member to at least  
28 one non-rigid member.

29  
30 Preferably said method of fabrication further comprises  
31 the step of forming at least one non-rigid member.

32



1 Preferably said step of forming said at least one non-  
2 rigid member comprises the step of high pressure plastic  
3 film forming with said high pressure acting on said  
4 apparatus.

5  
6 Alternatively said step of high pressure plastic film  
7 forming is arranged with the high pressure acting on a  
8 compliant membrane, which is part of a forming tool in  
9 contact with said apparatus.

10  
11 Preferably said rigid member has a maximum dimension  
12 perpendicular to its plane greater than the maximum  
13 dimension perpendicular to the plane of said at least one  
14 non-rigid member.

15  
16 According to a fifth aspect of the present invention,  
17 there is provided a method of mounting an apparatus for  
18 microfluidic processing applications, comprising the step  
19 of attaching said apparatus to a non-rigid carrier that  
20 is in the form of a tape.

21  
22 Preferably said carrier has a maximum dimension  
23 perpendicular to its plane greater than the maximum  
24 dimension perpendicular to the plane of said apparatus.

25  
26 Preferably said apparatus is attached to said non-rigid  
27 carrier by snap fitting into apertures in said carrier.

28  
29 Alternatively said apparatus is attached to said non-  
30 rigid carrier by ultrasonic welding, heat sealing,  
31 adhesive, chemical or molecular bonding.

32  
33 Preferably said apparatus is a tape.

1  
2 Preferably said apparatus comprises a polymer film.  
3  
4 Preferably said apparatus comprises processing elements  
5 for microfluidic processing.  
6  
7 Typically said processing elements comprise indents of  
8 said apparatus.  
9  
10 Optionally said processing elements comprise cavities  
11 embedded within said apparatus.  
12  
13 Optionally said processing elements comprise processing  
14 materials in intimate contact with the surface of said  
15 apparatus.  
16  
17 Optionally said processing elements comprise processing  
18 materials embedded within said apparatus.  
19  
20 Optionally said processing elements comprise opaque,  
21 translucent or coloured materials for providing optical  
22 isolation between elements or providing indexing marks.  
23  
24 Preferably an element of said apparatus is transparent.  
25  
26 Preferably a member of said apparatus is transparent.  
27  
28 Preferably said apparatus is penetrable.  
29  
30 Preferably said apparatus is self sealing during  
31 penetration.  
32

1 More preferably said apparatus is self sealing after  
2 penetration.

3

4 Preferably said apparatus further comprises an  
5 impermeable membrane.

6

7 Preferably said impermeable membrane is affixed in  
8 intimate contact with parts of the surface of said  
9 apparatus.

10

11 Alternatively said impermeable membrane is arranged as  
12 discrete areas of impermeable membrane in intimate  
13 contact with parts of the surface of said apparatus.

14

15 Preferably said impermeable membrane is penetrable.

16

17 Preferably said impermeable membrane is self sealing  
18 during penetration.

19

20 More preferably said impermeable membrane is self sealing  
21 after penetration.

22

23 Optionally said impermeable membrane is re-sealed by a  
24 capping element after penetration.

25

26 Preferably said impermeable membrane is supported by  
27 support structures.

28

29 Preferably said apparatus further comprises a non-rigid  
30 member.

31

32 Preferably said non-rigid member is affixed in intimate  
33 contact with parts of the surface of said apparatus.

1  
2 Alternatively said non-rigid member is arranged as  
3 discrete areas of non-rigid member in intimate contact  
4 with parts of the surface of said apparatus.  
5  
6 Preferably said non-rigid member is penetrable.  
7  
8 Preferably said non-rigid member is self sealing during  
9 penetration.  
10  
11 More preferably said non-rigid member is self sealing  
12 after penetration.  
13  
14 Optionally said non-rigid member is re-sealed by a  
15 capping element after penetration.  
16  
17 Preferably said non-rigid member is supported by support  
18 structures.  
19  
20 According to a sixth aspect of the present invention,  
21 there is provided a method of fabrication of an apparatus  
22 for mass transport microfluidic processing applications  
23 comprising the step of forming an apparatus that is non-  
24 rigid.  
25  
26 According to a seventh aspect of the present invention,  
27 there is provided a method of fabrication of an apparatus  
28 for mass transport microfluidic processing applications  
29 comprising the step of fabricating a tape.  
30  
31 Preferably said step of forming said apparatus comprises  
32 the step of high pressure plastic film forming with said  
33 high pressure acting on said apparatus.

1

2 Alternatively said step of high pressure plastic film  
3 forming is arranged with the high pressure acting on a  
4 compliant membrane, which is part of the forming tool in  
5 contact with said apparatus.

6

7 Optionally said step of fabricating said apparatus  
8 further comprises the step of preloading processing  
9 materials onto said apparatus before fabrication.

10

11 Optionally said step of fabricating said apparatus  
12 further comprises the step of loading processing  
13 materials onto said apparatus during fabrication.

14

15 Typically said step of preloading or loading during  
16 fabrication of said apparatus comprises the step of  
17 depositing processing materials onto a carrier.

18

19 Typically said step of preloading or loading during  
20 fabrication of said apparatus comprises the step of  
21 depositing processing material onto a non-rigid member.

22

23 Preferably said deposited processing material comprises  
24 permeation layers.

25

26 Alternatively said deposited processing material  
27 comprises conductive material.

28

29 Alternatively said deposited processing material  
30 comprises chemically or biologically active material.

31

32 Alternatively said deposited processing material  
33 comprises marks for identity purposes.

1  
2 Alternatively said deposited processing material  
3 comprises magnetisable material.  
4  
5 Preferably said step of depositing comprises printing.

6  
7 Alternatively said step of preloading or loading during  
8 fabrication of said apparatus is performed by a  
9 preloading or loading process selected from a list of  
10 processes comprising: deposition and etching, injection  
11 into a cavity and injection into an indentation.

12  
13 Preferably said method of fabrication of said apparatus  
14 further comprises the steps of depositing patterns on an  
15 apparatus and forming said apparatus, wherein the  
16 localised formation of said processing elements is  
17 responsive to the distortion by said forming of said  
18 deposited pattern.

19  
20 Preferably said method of fabrication of said apparatus  
21 further comprises the steps of depositing patterns on an  
22 apparatus and localised formation of said apparatus is  
23 responsive to the topography of said deposited pattern,  
24 resulting in the formation of said processing elements.

25  
26 Preferably said step of depositing comprises pre-  
27 printing.

28  
29 According to an eighth aspect of the present invention,  
30 there is provided a method of fabrication of an apparatus  
31 for mass transport microfluidic processing applications,  
32 comprising the step of including an impermeable membrane  
33 as part of said apparatus.

1  
2 Preferably said step of including an impermeable membrane  
3 comprises the step of affixing an impermeable membrane to  
4 a substrate.

5  
6 Optionally, said step of including an impermeable  
7 membrane comprises the step of depositing, overlaying or  
8 affixing discrete areas of impermeable membrane in  
9 intimate contact with parts of the surface of said  
10 apparatus.

11  
12 Optionally, said step of including an impermeable  
13 membrane comprises the step of depositing, overlaying or  
14 affixing an impermeable membrane on said apparatus and  
15 selectively removing areas of said impermeable membrane.

16  
17 Optionally, said selected removal of said impermeable  
18 membrane is performed by the step of cropping.

19  
20 According to a ninth aspect of the present invention,  
21 there is provided a method of fabrication of an apparatus  
22 for mass transport microfluidic processing applications,  
23 comprising the step of including a non-rigid member as  
24 part of said apparatus.

25  
26 Preferably said step of including a non-rigid member  
27 comprises the step of affixing a non-rigid member to a  
28 substrate.

29  
30 Optionally, said step of including a non-rigid member  
31 comprises the step of depositing, overlaying or affixing  
32 discrete areas of non-rigid member in intimate contact  
33 with parts of the surface of said apparatus.

1  
2 Optionally, said step of including a non-rigid member  
3 comprises the step of depositing, overlaying or affixing  
4 a non-rigid member on said apparatus and selectively  
5 removing areas of said non-rigid member.

6  
7 Optionally, said selected removal of said non-rigid  
8 member is performed by the step of cropping.

9  
10 According to a tenth aspect of the present invention,  
11 there is provided a method of microfluidic processing,  
12 comprising the steps of selecting an area of a plurality  
13 of areas of an apparatus and performing microfluidic  
14 processing at said selected area, characterised in that  
15 said apparatus is non-rigid.

16  
17 Optionally said step of performing microfluidic  
18 processing comprises contacting at least one conducting  
19 element that connects the exterior of said apparatus to  
20 the interior of said apparatus.

21  
22 Preferably said method further comprises the step of  
23 providing an electrical potential to at least one  
24 conducting element.

25  
26 Preferably said method further comprises the step of  
27 enabling an electrical current to pass through said least  
28 one conducting element.

29  
30 Preferably said apparatus is a tape.

31  
32 Preferably said microfluidic processing is mass transport  
33 microfluidic processing.



1

2 Preferably said microfluidic processing is responsive to  
3 the deformation of said apparatus.

4

5 Preferably said deformation comprises deformation by a  
6 step selected from a list of steps comprising: bending,  
7 flexing, folding, twisting, conforming to a rigid  
8 surface, mechanical deformation, deformation by applying  
9 a sound pressure, deformation by applying a liquid  
10 pressure, and deformation by applying a gas pressure.

11

12 Typically said gas pressure is a negative pressure.

13

14 Optionally said deformation may further comprise the step  
15 of bringing part of said apparatus back into contact with  
16 another part of itself.

17

18 Alternatively, said step of deformation further comprises  
19 the step of bringing a part of said apparatus into  
20 contact with another apparatus.

21

22 Optionally said deformation of said apparatus comprises  
23 the step of moving part of said apparatus into a position  
24 for processing of said part of said apparatus.

25

26 Typically said position for processing is a position with  
27 said apparatus in contact with a processing tool.

28

29 Preferably said microfluidic processing is responsive to  
30 said deformation of said apparatus, said microfluidic  
31 processing being selected from a list comprising pumping,  
32 filling, pouring, pressurising, mixing, dispensing,  
33 aspirating, separating, combining, heating and cooling.

1

2 According to an eleventh aspect of the present invention,  
3 there is provided a method of processing for microfluidic  
4 processing applications, characterised in that the  
5 processing comprises the step of piercing an impermeable  
6 membrane.

7

8 Preferably said step of piercing an impermeable membrane  
9 is performed with at least one probe.

10

11 Optionally said at least one probe comprises at least one  
12 pipette.

13

14 More preferably said method of processing further  
15 comprises the step of providing an electrical potential  
16 to at least one conducting probe that has pierced said  
17 membrane.

18

19 Alternatively said step of processing further comprises  
20 the step of enabling an electrical current to pass  
21 through at least one conducting probe that has pierced  
22 said membrane.

23

24 According to a twelfth aspect of the present invention,  
25 there is provided a method of processing for microfluidic  
26 processing applications, characterised in that the  
27 processing comprises the step of piercing an apparatus.

28

29 Preferably said apparatus is self sealing during said  
30 step of piercing.

31

32 Preferably said apparatus is self sealing after said step  
33 of piercing.

1  
2  
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33

Optionally said apparatus is re-sealed by a capping element after penetration.

Preferably said step of piercing the apparatus is performed with at least one probe.

Optionally said at least one probe comprises at least one pipette.

More preferably said method of processing further comprises the step of providing an electrical potential to at least one conducting probe that has pierced said apparatus.

Alternatively said step of processing further comprises the step of enabling an electrical current to pass through a conducting probe that has pierced said apparatus.

According to a thirteenth aspect of the present invention, there is provided an apparatus for microfluidic processing applications, characterised in that the apparatus is a non-rigid tape comprising a plurality of indexing patterns.

Preferably said indexing patterns are rigid members.

Preferably said indexing patterns are repeated.

Preferably said indexing patterns are arranged to facilitate detection of position.

1 Typically said indexing patterns are arranged to  
2 facilitate detection of position using optical detection.

3

4 According to a fourteenth aspect of the present  
5 invention, there is provided a method of transporting a  
6 tape apparatus for microfluidic applications comprising  
7 the step of moving said apparatus by interaction of a  
8 moving object with at least one rigid member attached to  
9 said apparatus.

10

11 In order to provide a better understanding of the present  
12 invention, an embodiment will now be described by way of  
13 example only and with reference to the accompanying  
14 figures in which:

15

16 Figure 1 illustrates in schematic form non-rigid  
17 apparatuses, showing a section of tape and an enlargement  
18 of one area suitable for gel electrophoresis in  
19 accordance with the present invention;

20

21 Figure 2 illustrates in schematic form a variety of  
22 processing elements in accordance with the invention;

23

24 Figure 3 illustrates processing elements incorporating  
25 impermeable membranes comprising homogeneous apparatus  
26 material;

27

28 Figure 4 illustrates impermeable processing elements  
29 incorporating discrete impermeable membranes and  
30 processing elements on hinged tabs;

31

1 Figure 5 illustrates the insertion and removal of a probe  
2 into a processing element through an impermeable self-  
3 sealing membrane;

4

5 Figure 6 illustrates a plan view of an apparatus  
6 incorporating an extended impermeable membrane with a  
7 variety of support structures;

8

9 Figure 7 illustrates a cross-section of the same  
10 structures illustrated in Figure 6;

11

12 Figure 8 illustrates some of the same structures in  
13 cross-section as Figure 7, but where the processing  
14 elements comprise processing materials;

15

16 Figure 9 illustrates in schematic form a plan view of a  
17 structure for probing through an impermeable membrane;

18

19 Figure 10 illustrates an alternative arrangement to that  
20 of Figure 9 where the channel extends into the apparatus;

21

22 Figure 11 illustrates a cross-section of the structure  
23 illustrated in Figure 10;

24

25 Figure 12 illustrates a tape apparatus with indexing  
26 patterns;

27

28 Figure 13 illustrates in schematic form a variety of  
29 cross-sections of indexing patterns;

30

31 Figure 14 illustrates a flow chart describing the steps  
32 of fabrication of an apparatus;

33

1 Figures 15 and 16 illustrate arrangements of scanning the  
2 optical detectors for scanning the apparatus;

3

4 Figure 17 illustrates plan and elevation views of a  
5 micro-array configuration of the apparatus;

6

7 Figure 18 illustrates in schematic form non-rigid  
8 apparatuses in accordance with the present invention;

9

10 Figure 19 illustrates in schematic form the components of  
11 a planned fabrication scheme of one embodiment;

12

13 Figure 20 illustrates in schematic form a compact  
14 fabrication option;

15

16 Figure 21 illustrates in schematic form an operating mode  
17 using a vacuum suction onto a scanner or a  
18 heating/cooling plate;

19

20 Figure 22 illustrates in schematic form reservoir  
21 fabrication showing the option of sample loading through  
22 penetration of a cover seal;

23

24 Figure 23 illustrates in schematic form reservoir  
25 fabrication showing the option of electrical probe  
26 penetration of a cover seal;

27

28 Figure 24 illustrates in schematic form an alternative  
29 electrical probe option;

30

31 Figure 25 illustrates in schematic form a supporting  
32 layer of one segment of a tape after preparatory  
33 printing;

- 1
- 2 Figure 26 illustrates in schematic form a formed pattern
- 3 layer after forming;
- 4
- 5 Figure 27 illustrates in schematic form a formed pattern
- 6 layer after a blanking operation;
- 7
- 8 Figure 28 illustrates in schematic form a formed pattern
- 9 layer assembled to the supporting layer;
- 10
- 11 Figure 29 illustrates in schematic form an exoskeleton;
- 12
- 13 Figure 30 illustrates in schematic form an exoskeleton
- 14 affixed to the supporting/patterned layer;
- 15
- 16 Figure 31 illustrates in schematic form a section
- 17 (vertical scale exaggerated for clarity) and plan view
- 18 through one tape segment and disposition of sealing
- 19 plugs;
- 20
- 21 Figure 32 illustrates in schematic form loading of
- 22 electrolyte during manufacture;
- 23
- 24 Figure 33 illustrates in schematic form loading of
- 25 analyte during manufacture; and
- 26
- 27 Figure 34 illustrates in schematic form loading of a test
- 28 sample at the point of use.
- 29
- 30 Figure 35 illustrates in a flowchart of automated
- 31 processing using the fabricated tape.
- 32

1 The invention is a non-rigid apparatus for microfluidic  
2 processing applications, which may be in the form of a  
3 tape. The use of a non-rigid apparatus allows novel  
4 dynamic processing methods. The incorporation of re-  
5 sealable impermeable layers allows further novel dynamic  
6 processing steps.

7  
8 Figure 1a shows a typical section of tape 1 with an array  
9 of microfluidic processing areas or processing segments 2  
10 in accordance with a preferred embodiment of the present  
11 invention. Adjacent test segments are spaced to suit the  
12 sample supply vessel. For example, where samples are  
13 delivered for test in a 384 well microtiter plate format,  
14 the tape segments will be supplied on a 4.5mm pitch, P.  
15 The tape is processed in a vertical plane with the sample  
16 loading ports uppermost. The tape width, W, is typically  
17 25mm but is configurable in a range of 1mm to 100mm.

18  
19 Figure 1b shows an enlargement of a single processing  
20 segment 2, the operation of which follows well-  
21 established principles of electrophoresis. A DNA test  
22 sample is assumed.

23  
24 The apparatus includes a supporting layer 251, a formed  
25 pattern layer 265 with a machine readable index mark 254.  
26 The pattern layer has formed cavities 266 and a  
27 connecting channel 267 filled with gel. The exoskeleton  
28 2915 supports plugs 3124 that are used for re-sealable  
29 access to the cavities.

30  
31 A DC voltage in the range 5 to 500 Volts (typically  
32 100V/cm has been found to be suitable) will be applied  
33 across negative terminal 252 and positive terminal 253.



1 This will cause the negatively charged DNA sample 3430 to  
2 migrate into the gel column 267 and its constituent  
3 molecules will then separate into bands in accordance  
4 with their molecular weight. An image of the band pattern  
5 will be captured by a commercial CCD camera and the image  
6 processed and presented to the user on a computer screen.

7  
8 The electrical terminal pads 252 and 253 are conveniently  
9 presented for perpendicular access by external contact  
10 pins whose engagement will be controlled by the tape  
11 processing instrument. The exoskeleton 2915 may be  
12 conveniently employed as the tape transport means, and be  
13 driven by, for example, a toothed belt or a drive pinion  
14 having the same tooth pitch as the test segments on the  
15 tape.

16  
17 The CCD image capture system can also conveniently  
18 capture the test segment ID mark, thus avoiding the need  
19 for a separate device such as a bar code reader.

20  
21 Figure 2a illustrates a part of an apparatus 20 in cross-  
22 section. The apparatus contains a variety of processing  
23 elements which are an indent 21, a void or cavity in the  
24 apparatus 22 processing materials on the surface of the  
25 apparatus 23, processing materials embedded within the  
26 apparatus 24, and processing materials in an indent on  
27 the surface of the apparatus 25.

28  
29 Figure 2b illustrates part of an apparatus in cross-  
30 section with processing materials partially filling the  
31 height of a cavity in the apparatus 26 and processing  
32 material 27 embedded in a channel 28 within the  
33 apparatus.

1  
2 The processing elements may comprise geometries which  
3 have sloping, curved or stepped surfaces. The processing  
4 materials may be conformal layers in intimate contact  
5 with surfaces of the apparatus. The processing elements  
6 may be opaque, translucent or coloured in order to  
7 provide optical isolation between elements or,  
8 alternatively, to provide indexing marks for allowing  
9 detection of movement and position of the apparatus.

10  
11 Several of the processing elements shown in Figures 2a  
12 and 2b may be linked together, for example by cavities  
13 or indented troughs, which are themselves processing  
14 elements such that the linked elements act as a single  
15 processing group.

16  
17 Figure 2c illustrates a plan view 210 of processing  
18 element groups 211 on part of an apparatus 212. Figure  
19 2d illustrates a cross section of one of the processing  
20 element groups 211 shown in figure 2c. The formed  
21 plastic substrate 212 has a plastic membrane film 213  
22 attached 214. The membrane is typically 0.1mm thick, but  
23 could be as thin as 0.02mm. An indented trough 215 is  
24 provided for processing materials such as materials based  
25 on Agarose or polyacrylamide gel. A channel 216 is  
26 provided for a plug that can be removed by, for example,  
27 laser ablation in order to allow processing material  
28 transport between the indented trough 215 and another  
29 processing element, indent 217. The substrate indents  
30 have pips 218 that are shaped to guide a probe such as a  
31 pipette to an area of the lower surface for penetration  
32 into the processing elements, for example indent 217.

1 The substrate may be self-sealing during and after such  
2 penetration.

3

4 The processing materials can be gases, liquids, solids or  
5 semi-solids, e.g. biomolecular samples, fragments of  
6 DNA, biochemical polymers, chemical polymers,  
7 biomolecular modifiers, catalysts, antibodies,  
8 polypeptide molecules, protein molecules, biological  
9 organisms such as cells and viruses and permeation  
10 layers. The permeation layers may be solid, semi-solid,  
11 liquid, viscous, gelatinous or gaseous layers. The  
12 permeation layers may be biomolecular gates which are  
13 activated by electrical probes. The function of the  
14 biomolecular gates is defined by their particular depth,  
15 shape, volume and composition.

16

17 Figure 3 shows a cross-section 30 of an apparatus for  
18 microfluidic processing applications. The apparatus  
19 contains a processing element 31 that is a cavity in the  
20 apparatus material. At the top of the cavity the  
21 apparatus material is thin, such that there is a membrane  
22 32 that is impermeable and acts as an hermetic seal to  
23 protect the contents of the cavity.

24

25 The apparatus contains another processing element 33,  
26 where the membrane is configured as a flap 34, such that  
27 the cavity is sealed when the unattached end of the  
28 membrane is in contact with the apparatus 35.

29

30 Figure 3 illustrates another processing element 36 with a  
31 membrane arranged as a flap 37 and distortion of the  
32 apparatus 38 resulting in the opening of the flap at its  
33 unattached end 39.

1  
2 Figure 4a illustrates an apparatus 40 that includes the  
3 same type of processing elements as shown in Figure 3,  
4 but in this case the impermeable membrane is deposited,  
5 overlaid or affixed as discrete areas of impermeable  
6 membrane in intimate contact with parts of the surface of  
7 the apparatus. In the first processing element 41, the  
8 impermeable membrane 42 provides a hermetic seal to the  
9 cavity 43.

10  
11 Another processing element 44 shows the impermeable  
12 membrane 45 in intimate contact and attached to the  
13 apparatus at the left hand side 46 and configured as a  
14 flap in a sealing contact with the right hand side 47 of  
15 an indent in the apparatus 48. This flap may be opened  
16 by deforming the apparatus in the same way as described  
17 as above with reference to processing element 36.

18  
19 In another processing element 49, the impermeable  
20 membrane 410 is deposited as a plug in an indent  
21 resulting in a cavity 411, the membrane again providing  
22 an hermetic seal.

23  
24 Alternatively, the impermeable membrane is continuous  
25 with the tape (i.e. not discrete). This continuous  
26 configuration can also embody local flaps in the membrane  
27 and still be one continuous membrane.

28  
29 Figure 4b illustrates a plan view and Figure 4c  
30 illustrates cross-section views of a strip of apparatus  
31 413 where a section of the apparatus had been removed 412  
32 by punching out. The shape punched out has left several  
33 tabs 414 each with an indent 415 for containing

1 processing materials. The tab 414 may be mechanically  
2 folded along the fold line 417. The fold line may be  
3 weakened by perforation or indenting. A second indent  
4 for processing materials 418 is positioned on the  
5 opposite side of the fold line from the indent 415. When  
6 the tab is folded over 419, the indent 415 is tipped over  
7 into contact with the indent 418, allowing mixing,  
8 pouring or transfer of processing materials between the  
9 two indents. This pouring may be assisted by the force of  
10 gravity, capillary action or external pressure.  
11 Alternative arrangements can be made that tilt through an  
12 angle of e.g. 30 degrees to cause pouring.

13  
14 Figure 5 shows a cavity during a sequence of steps before  
15 penetration 51, during penetration 52 and after  
16 penetration 53. The probe 54, which is a pipette, is to  
17 be inserted into the cavity 55 through the membrane 56.  
18 When the probe 57 is inserted through the membrane 58,  
19 the membrane is self-sealing, such that there is a seal  
20 between the probe and the membrane 58. Processing  
21 materials 510 are then deposited in the cavity. After  
22 removal of the probe 511, the impermeable membrane is  
23 self-sealing and a seal 512 is formed at the exit point  
24 of the probe. The penetration of the impermeable  
25 membrane can allow introduction of processing materials  
26 into cavities in the apparatus or removal of processing  
27 materials from the apparatus, the penetration of the  
28 membrane can allow the introduction of measurement tools  
29 into the apparatus or processing tools into the  
30 apparatus. When penetration is by a conducting probe,  
31 voltages can be applied that cause movement of fluids  
32 through processing materials using an electrokinetic  
33 method.

1  
2 Large areas of membrane would tend to bend on attempted  
3 insertion of a probe. Figure 6 shows a plan view of an  
4 apparatus 60 with an extended membrane 61 and support  
5 structures that provide support for the membrane adjacent  
6 to the location where probes are to penetrate the  
7 membrane. Figure 7a shows a cross-section 70 of the same  
8 structure that is shown in the plan view of Figure 6.  
9 Figure 7b shows a cross-section 71 of the same structure  
10 that is shown in the plan view of Figure 6, but with a  
11 continuous membrane 72 affixed to a substrate.

12  
13 Figures 6 and 7 include support structures that are  
14 pillars 62, ribs 63 and an annulus 64. The centre of the  
15 annulus contains a membrane that may be penetrated by a  
16 probe. The annulus allows a "via" hole 65 to be created  
17 all the way through the apparatus and through which a  
18 wire or conducting probe can be passed so that a magnetic  
19 field can be created to interact with the adjacent  
20 processing area of the apparatus.

21  
22 Another useful structure is a circular indent but still  
23 connected to adjacent processing elements and an  
24 externally configured loop or coil of wire (or other  
25 conducting element) around that circular indent. The  
26 electrical/magnetic field created can be used to attract  
27 or trap or process the liquid in the circular indent.

28  
29 A "U" shaped pillar 66 is shown and a probe that enters  
30 in the centre of the "U" at point 67, marked with a plus,  
31 may be connected to a probe penetrating the impermeable  
32 membrane at the second penetration point 68 by an  
33 electrical, liquid or permeation path that is greater in

1 length than the direct distance between the two  
2 penetration points.

3

4 Figure 8 shows a cross-section 80 of similar structures  
5 to those in Figure 7, except that the cavities in the  
6 apparatus are filled with processing materials 81.

7

8 Figure 9 shows a plan view of an apparatus 90 with a  
9 membrane that extends from a first penetration point 91  
10 to a second penetration point 92 via an indented trough  
11 93. A probe inserted through the impermeable membrane at  
12 the first penetration point 91 may be connected to a  
13 probe penetrating the impermeable membrane at the second  
14 penetration point 92 by an electrical, liquid or  
15 permeation path that is greater in length than the direct  
16 distance between the two penetration points.

17

18 Figure 10 shows a plan view of an apparatus 100 with two  
19 membranes, each of which are penetration points 101 and  
20 102. The dotted lines represent the edges of a buried  
21 channel 103 in between the two membranes.

22

23 Figure 11 shows a cross-section through the line  
24 connecting the two penetration points of Figure 10 which  
25 can be seen to be two membranes 101 and 102. The channel  
26 103 extends into the depth of the apparatus 104. In this  
27 alternative arrangement the electrical, liquid or  
28 permeation path between tips of probes that are inserted  
29 through the penetration points are also greater than the  
30 direct distance between the two probes.

31

32 Turning Figures 10 and 11 through 90 degrees, illustrates  
33 side entry (rather than top entry) to the apparatus.

1 Then Figure 10 becomes a side view of the tape and Figure  
2 11 is a plan view of the plane of a strip of tape.

3  
4 With reference to Figure 12, an apparatus 120 is shown in  
5 plan view with a plurality of indexing patterns 121. The  
6 indexing patterns may be opaque, translucent or coloured  
7 materials. The indexing patterns may be surface  
8 patterns, such as indents or process materials or raised  
9 patterns of apparatus material, for example the  
10 exoskeleton (2915 in Figures 1b and 29). Alternatively,  
11 the indexing patterns may be embedded within the  
12 apparatus or patterns of magnetism in a magnetic film or  
13 perforations through the depth of the apparatus. Indexing  
14 patterns are arranged to facilitate traction of the  
15 apparatus and detection of position using optical,  
16 electromagnetic, electrochemical, electrical or other  
17 forms of detection. The indexing patterns may also  
18 record information related to the apparatus processing  
19 elements or the apparatus processing materials on the  
20 apparatus or within it processing results, processing  
21 status, processing time, processing location or  
22 processing identity. An indexing pattern may be a strip  
23 of material which functions as a data recording medium,  
24 for example magnetic or magneto-optical tape. Such tape  
25 may be written to and read by standard methods.

26  
27 With reference to Figure 13 that shows in schematic form  
28 a variety of cross-sections of indexing patterns, an  
29 indexing pattern is shown as an indent 130, a raised  
30 feature 131, an embedded feature 132 or a hole 133  
31 punched through the apparatus.

32



1 With reference to Figure 14a, a flow chart is shown which  
2 describes the general process steps for the fabrication  
3 of non-rigid apparatuses for microfluidic processing  
4 applications, including apparatuses in the form of a tape  
5 or apparatuses of homogeneous material which may be  
6 assembled to a tape or discrete microfluidic devices  
7 which may be assembled to a tape.

8  
9 Firstly, raw material preparation is provided, 141, the  
10 primary material will be a flexible substrate, preferably  
11 in the form of a continuous tape but other substrates,  
12 membranes, films, mouldings, skeletal structures or pre-  
13 assembled microfluidic devices may be part of the  
14 fabrication "kit".

15  
16 Patterns can be pre-printed 142, preferably on a flat  
17 plastic non-rigid substrate. These patterns may be  
18 conductive elements, chemically or biologically active  
19 zones, magnetisable zones, or printed marks for identity  
20 purposes.

21  
22 The apparatus, 143, is formed using high pressure thermo-  
23 forming with the high pressure acting on the apparatus or  
24 the high pressure acting on a compliant membrane which is  
25 part of the forming tool that is in contact with the  
26 apparatus. The high pressure may be delivered by a gas  
27 or a fluid. During forming, the pre-printed patterns on  
28 the tape surface may be distorted in response to the  
29 topography of the formed processing elements. The final  
30 position of the pre-printed pattern material may be  
31 predicted by calibration test runs or simulation in order  
32 to design pre-printed patterns that distort to create  
33 processing elements that comprise the processing material

1 that has been pre-printed. Alternatively, the forming of  
2 an apparatus may be performed by stereolithography or  
3 selective laser sintering. While forming the apparatus  
4 by stereolithography or selective laser sintering,  
5 processing elements may be included in the apparatus  
6 either by direct patterning or in response to the  
7 topography of the pre-printed patterns on the carrier.

8  
9 The fabrication of the apparatus can further comprise the  
10 step of preloading processing materials 144. These  
11 processing materials may be preloaded by processes such  
12 as printing, film deposition and etching, stereo-  
13 lithography, injecting into a cavity and also injection  
14 into an indentation. Alternatively, the preloading may  
15 be achieved by tilting the apparatus with respect to  
16 gravity in order to open flaps of impermeable membrane so  
17 as to introduce processing materials through the open  
18 flaps into underlying structures. Alternatively these  
19 flaps may be opened by the distortion of the apparatus,  
20 such as conforming it to a rigid roller or corner.

21  
22 A cropping operation 145 can be incorporated (optionally  
23 before the preloading step) to insert apertures in a  
24 substrate or finish a substrate to a defined external  
25 profile.

26  
27 Apparatus assembly can continue, 146, by attachment or  
28 assembly of other layers, for example, a sealing layer or  
29 sealing layers, or sealing plugs, or additional  
30 supporting layers to improve the robustness of the  
31 apparatus, or other pre-assembled devices. The attachment  
32 methods may include a mechanical snap-fit, a mechanical  
33 interference fit, ultrasonic welding, heat sealing,

1 molecular, chemical or adhesive bonding. Typically the  
2 final layer of apparatus that is affixed results in one  
3 or more impermeable membranes as part of the apparatus.  
4 Alternatively, the membranes may be formed by depositing,  
5 overlaying or affixing discrete areas of impermeable  
6 membrane in intimate contact with parts of the surface of  
7 the apparatus. Alternatively the formation of the  
8 impermeable membrane may be performed by depositing a  
9 film of impermeable membrane across the apparatus and  
10 selectively removing areas of the impermeable membrane.  
11 This selective removal may be performed using  
12 cropping/blanking or by lithography, such as  
13 photolithography, for patterning combined with wet or dry  
14 etching. These membranes are optionally formed of  
15 homogeneous apparatus material in the case of formation  
16 using stereo-lithography or selective laser sintering.  
17  
18 The apparatus can incorporate a further loading sequence,  
19 147, of chemical or biological agents such as solvents,  
20 electrolytes, gels, stainers, dyes, affinity tags or bio-  
21 sensors. This loading may be achieved by pipette probe  
22 through the apparatus membrane or through an access port  
23 or access ports in the apparatus.  
24  
25 These steps 141 to 147 have many possible permutations  
26 and Figures 14b, 14c and 14d illustrate by way of  
27 example, the fabrication sequence of some of the  
28 alternative embodiments described within this document.  
29  
30 Figure 14b shows the general fabrication sequence for the  
31 three layer construction method described by Figure 19  
32 including the fabrication steps 14191, 14192 and 14193 of

1 the substrate 191 sealing layer 192 and carrier layer 193  
2 respectively.

3

4 Figure 14c shows the general fabrication sequence for the  
5 three layer construction method described by Figure 22,  
6 including the fabrication steps 14221, 14222 and 14225 of  
7 the substrate 221 sealing layer 222 and carrier layer 225  
8 respectively.

9

10 Figure 14d shows the general fabrication sequence for the  
11 construction method described by Figure 1b including the  
12 fabrication steps 14251, 14265, 142915 and 143124 of the  
13 substrate 251 process layer 265, exoskeleton 2915 and  
14 sealing caps 3124 respectively.

15

16 In each of Figures 14a to 14d, the material preparation  
17 step 141 is a film forming step, except for the  
18 exoskeleton and sealing cap material preparation 1411,  
19 which is a moulding step.

20

21 With reference to Figure 15, the moving apparatus 150  
22 with indexing patterns that are permeation (for  
23 separation) indents 151, can provide the scanning  
24 function of a scanning optical detector with fixed optics  
25 152 and a fixed line scan Charged Coupled Device (CCD)  
26 detector 153.

27

28 Additionally, with reference to Figure 16, when this  
29 fixed scanning system 161 is configured to suit a chosen  
30 width of tape apparatus 162 (e.g. 100mm, shown in plan  
31 view, not to scale) or multiple transverse separation  
32 layers, then it can also image capture, without  
33 modification, any other tape apparatus which is of lesser

1 width 163 (e.g. 50mm or 20mm), thus providing the  
2 advantage of a detection system with flexibility in the  
3 handling of different widths of substrate.  
4

5 Additionally, where the substrate is configured to have  
6 more than one discrete permeation layer in a transverse  
7 line across the substrate, each of these more than one  
8 discrete permeation layers can be imaged simultaneously.  
9

10 In the emerging field of biological micro-arrays, the  
11 processing substrates are typically comprised of a rigid  
12 transparent material (e.g. a glass slide) and whereby  
13 bio-material is deposited locally on a rectangular grid  
14 whose pitch may be in the range of 50um to 2mm. The  
15 present invention provides the advantage that it is  
16 equally suitable as a substrate for micro-array  
17 fabrication but offers the benefit of having low  
18 fabrication cost and a capability for continuous  
19 processing due to the flexible nature of the apparatus in  
20 its form as a continuous tape.  
21

22 With reference to Figure 17, the apparatus is illustrated  
23 schematically 170 in plan and side views configured to  
24 locate each element of a micro-array 171 in a shallow  
25 well or dimple 172, on a tape 173, thereby allowing a  
26 reduced risk of cross contamination between adjacent  
27 elements.  
28

29 The apparatus is thus configured to provide an improved  
30 degree of containment for any reaction process which is  
31 specified to take place on that micro-array element and  
32 that this improved degree of containment can allow

1 operations of mixing, stirring or agitation which would  
2 not be achievable with planar micro-arrays.

3  
4 The apparatus is configured such that this shallow well  
5 has a thin wall section 174 (e.g. 0.1mm, compared to a  
6 glass slide of typically 1 to 3mm) that enables the  
7 efficient coupling of a conductive heating element 175  
8 (for example a peltier device or similar) to the well for  
9 the purpose of, for example, hybridisation of a DNA  
10 sample at a temperature in the range of, for example, 60  
11 to 80 degrees centigrade.

12  
13 This thin wall section can readily be transparent and  
14 that this enables the efficient coupling of an optical  
15 system 175 to detect the bio-reaction state of any  
16 element on the micro-array.

17  
18 The apparatus can also have different regions  
19 functionalised for the attachment of chemical or  
20 biological moieties such as affinity tags or biological  
21 probes. Within a microfluidic channel, there can be  
22 micro-zones incorporating reactive groups for highly  
23 specific functions, e.g. an affinity tag such as a  
24 streptavidin coated zone.

25  
26 With reference to Figure 18, an apparatus 10 according to  
27 the present invention is shown. The apparatus 11 is non-  
28 rigid and is shown as being bent, by the apparatus being  
29 conformed to the surface of a roller 12.

30  
31 The apparatus is non-rigid in that it is pliant, unlike  
32 rigid apparatuses known in the prior art that are made of  
33 at least one layer of hard plastic or glass or silicon,

1 or where the composite apparatus is rigid. On  
2 deformation of the apparatus according to the present  
3 invention, the apparatus can return to its original shape  
4 (i.e. flat) after deformation. The apparatus may have a  
5 bend radius approaching zero.

6  
7 The apparatus is a tape in that it is substantially  
8 longer than it is wide in its larger two dimensions.  
9 Hence it is a substantially continuous, narrow, flexible  
10 strip. The tape 13 may be arranged in a reel-to-reel  
11 arrangement between reels or rollers 14 and 15.

12  
13 With extreme deformation, the apparatus may be folded and  
14 remain folded. This may be facilitated by using  
15 perforations or indentations to weaken the fold line.  
16 Thus the apparatus may be folded into a fanfold  
17 arrangement 16 for storage, dispensing and processing.

18  
19 The tape can also be separated into short discrete  
20 sections 17. The separation may be performed by  
21 guillotining or tearing across perforations or  
22 indentations in the tape.

23  
24 A continuous strip of tape 18 may be arranged around  
25 rollers 19 into a conveyor belt arrangement. A twist in  
26 the tape would provide a Moebius strip arrangement.

27  
28 The apparatus may be formed from a polymer film, that is  
29 a thermoplastic polymer film, thermosettable polymer  
30 film, elastomeric polymer film or hybrid compositions of  
31 each of these films.

32

1 In another embodiment, the tape comprises three primary  
2 construction elements as illustrated with reference to  
3 Figure 19. The tape incorporates a thin polymer substrate  
4 191 that is formed to create indented wells, channels and  
5 junctions which can be configured to create a wide range  
6 of micro-fluidic geometries. This substrate may  
7 optionally incorporate one or more surface coating layers  
8 on the processing side of the substrate and these  
9 layer(s) may fully cover the substrate surface or be  
10 confined to local areas of the substrate. The substrate  
11 may incorporate liquid or solid chemicals within the well  
12 or channel areas of the substrate.

13  
14 The substrate and its chemical contents may be protected  
15 by the attachment of a cover seal 192 membrane. The  
16 combined substrate and cover seal will be attached to a  
17 carrier layer 193 whose function is to protect the  
18 substrate from mechanical stress or damage during  
19 handling, shipment, storage or end user processing. The  
20 tape may be a one time use consumable item.

21  
22 The tape assembly employs construction materials,  
23 fabrication techniques and packaging methods that ensure  
24 that the tape will function reliably at its final point  
25 of use. The tape will therefore be unaffected by:  
26 - Automated and manual handling processes prior to  
27 shipment packaging (factory);  
28 - Automated and manual handling processes at the point of  
29 use (end user);  
30 - Shipment transport (protected by secondary packaging);  
31 - Transport temperatures of -40C to +70C (up to 24  
32 hours);  
33 - Storage temperatures of 0C to +40C (up to 12 months);



- 1 - Relative humidity in range 10% to 90% (transport and  
2 storage); and  
3 - Atmospheric pressure (air cargo).  
4

5 The substrate comprises a thin polymer membrane with a  
6 thickness of 50um preferred, but 125um for some  
7 applications. The thickness may be selected to match  
8 available commercial film grades.  
9

10 The substrate has:

- 11 - Forming radius equal to thickness without stress  
12 cracking;  
13 - Feature width to depth ratio, typically in range 2:1 to  
14 1:1;  
15 - Uniform (consistent) draw during forming.  
16

17 Thermal assist during (or prior to) forming is desirable.

18 Forming may be:

- 19 1) high pressure in range 1 bar to 200 bar  
20 2) Vacuum  
21 3) high pressure with vacuum assistance  
22  
23

24 All of these may benefit from a pre-heating cycle.  
25

26 Desirable features of the substrate include:

- 27 - stable after forming (having no shape memory effects );  
28 - Flexible, non rigid, non brittle;  
29 - Abrasion Resistant;  
30 - Punchable, to create optional holes for mechanical  
31 indexing;  
32 - Penetratable by probe (e.g. for liquid delivery or for  
33 electrical probing);

- 1 - High optical clarity;
- 2 - Adaptable via suitable surface modification to minimise
- 3 static charge or to locally influence
- 4 hydrophilic/hydrophobic surface characteristics;
- 5 - Chemical Resistance to Aqueous solutions
- 6 - Analyte material loaded in the substrate channels
- 7 typically comprised of Agarose or Polyacrylamide,;
- 8 - Provide bio-compatible surface (e.g. DNA, proteins,
- 9 cells, bacteria etc);
- 10 - Avoid leeching of metals, anti-oxidants and
- 11 stabilisers;
- 12 - Capable of receiving a heat sealable cover layer e.g.
- 13 polyester/polyethylene cover layer; and
- 14 - Printable with ink, stroke widths down to 0.1mm.
- 15
- 16 Auxiliary coatings or deposited layers on the substrate
- 17 include:
- 18 - Local conductive tracking;
- 19 - Local hydrophobic coatings (e.g. PTFE);
- 20 - Local hydrophilic coatings (eg titanium oxide); and
- 21 - Bio-compatible coatings (e.g. parylene).
- 22
- 23 The seal 192 may be a single or composite layer but a
- 24 dual composite construction may be beneficial in that the
- 25 outer layer can be specified to resist the thermal
- 26 affects of the heat sealing tool whereas the inner layer
- 27 is able to melt and create a seal without putting the
- 28 integrity of the membrane at risk. Properties of the seal
- 29 layer include:
- 30 - Seal Thickness: Typically in range 10um to 50um;
- 31 - Chemical Resistance: As per substrate above;
- 32 - Optical: As per substrate above;
- 33

1 It is preferred that the seal be suitable for penetration  
2 by a probe (typically 0.5-1mm diameter) e.g. for liquid  
3 delivery or for electrical probing. A self healing or re-  
4 sealable penetration hole is preferred.

5  
6 Pre-forming of the seal (schematically as in Figures 22  
7 and 23) is optional to enhance rigidity of the sealing  
8 layer during penetration and to provide the necessary  
9 space within the tape for processing materials.

10  
11 The carrier layer 193 can comply with EIA-481-B  
12 (Electronic Industries Alliance), the standard for  
13 "Embossed carrier Taping" for automated component  
14 handling in the electronic industries. A preferred  
15 material is either black or translucent polystyrene,  
16 preferred thickness is in the range 100um to 300um. This  
17 layer will be formed prior to assembly of the  
18 substrate/cover such that the substrate/cover will be  
19 contained within a recessed channel in the carrier tape  
20 and thereby avoid contact with any other surfaces during  
21 manufacture or distribution (e.g. in a reel), or at point  
22 of use.

23  
24 The primary functions of the carrier layer are a) to  
25 provide a mechanically robust carrier for the more  
26 fragile substrate/cover layers b) incorporate punched  
27 holes which provide a means of transport drive for the  
28 tape c) incorporate registration features which align the  
29 substrate/cover layer with the punched drive holes d)  
30 incorporate apertures which allow the channels in the  
31 substrate to be visible from underneath the tape.

32

1 With reference to Figure 20, which is a section across  
2 the width of the tape, not to scale, a 50um thick  
3 microfluidic substrate 201 formed up to 250um deep, is  
4 contained within the 300um thickness of the carrier 202  
5 thus affording it protection. The substrate has analyte  
6 203 and is capped with the seal 204.

7  
8 With reference to Figure 21, a negative pressure (vacuum)  
9 is applied to the two ports 210 that distorts the  
10 substrate onto a tool 211 such as a viewing window of a  
11 scanner or a heating/cooling plate.

12  
13 With reference to Figure 22, a sample loading probe 221  
14 is positioned ready to penetrate a reservoir in the pre-  
15 formed cover seal 222 (that is dimpled for ease of  
16 insertion). The substrate contains analyte 223 and the  
17 reservoir contains electrolyte 224.

18  
19 With reference to Figure 23, electrokinesis 231 probes  
20 are shown penetrating the reservoirs.

21  
22 With reference to Figure 24, probes 241 external to the  
23 "wet chemistry" zone are shown connecting to conductive  
24 layers on the substrate that are an anode 242 and a  
25 cathode 243.

26  
27 For the preferred embodiment, a single segment of tape  
28 will be described below, comprising the means of  
29 processing one discrete test sample of bio-material such  
30 as DNA.

31  
32 Figure 25 shows a supporting layer 251 comprises a thin  
33 flat optically clear film of either polycarbonate,

1 polyester, polystyrene, poly methyl methacrylate, or  
2 other co-polymers of these materials. This film will  
3 typically be 125um thick but other thicknesses in the  
4 range 25um to 1000um may be used. This Layer has a  
5 pattern of conductive tracks 252 and 253 applied by  
6 screen printing or laser printing or ink jet printing as  
7 well as a pattern 254 which can be machine read to  
8 indicate the identity of that segment.

9  
10 Figure 26 shows a formed patterned layer 265 comprising a  
11 thin film of either polycarbonate, polyester,  
12 polystyrene, polyethylene, polymethyl methacrylate,  
13 polypropylene or other co-polymers of these materials.  
14 This film will be typically 50um thick but other  
15 thicknesses in the range 10um to 200um may be used. This  
16 material need not be optically transparent and some  
17 advantage may be gained by having it translucent or  
18 opaque; translucency offers a means of back-lighting  
19 scatter (opposite side from the optical supporting layer)  
20 which may be used for illuminating and capturing an image  
21 of the tape processes; opaqueness offers the possibility  
22 of using a reflected front-lighting source.

23  
24 High pressure thermoforming is preferably used to create  
25 formed cavities 266, connecting channels 267, optional  
26 side channels 268, primary access ports 269 and secondary  
27 optional access ports 2610 . Shallow channels 2611  
28 provide entry slots for the conductive tracks 252, 253.  
29 Typical relative depths of these formed features is  
30 illustrated in typical section Figure 31.

31  
32 Figure 27 shows a further preparative step in  
33 manufacturing the formed patterned layer whereby a

1 knifing or blanking process is used to cut apertures or  
2 slots in the film. Apertures 2712 provide the access  
3 entry slots for the conductive tracks 252, 253. Aperture  
4 2713 ensures that the code mark 254 is not obscured by  
5 any translucency or opaqueness in the film 265.  
6

7 Figure 28 shows layer 251 and layer 265 assembled  
8 together. This will be effected by either a heat sealing  
9 or an adhesive process or both, to ensure that the two  
10 layers achieve a tight seal around the profile of the  
11 various patterned recesses 266, 267, 2611 etc. in Layer  
12 265. Heat sealing can be achieved by the contact surface  
13 material of Layer 265 comprising a thin layer of low  
14 melting point polymer such as poly-ethylene;  
15 alternatively adhesive bonding can comprise the use of  
16 commercial cyano-acrylate or, in the case of sealing  
17 zones 2814, a commercial silicone rubber compound may be  
18 used.  
19

20 Figure 29 shows an exoskeleton component 2915 whose  
21 purpose is to protect layer 265 as well as providing  
22 rigid access ports 2916, 2917 for loading and unloading  
23 the tape. Apertures 2918 protect the cavities 266 and an  
24 aperture 2919 protects the channel 267.  
25

26 The exoskeleton material is preferably a rigid polymer  
27 such as polycarbonate, ABS, polyester, polystyrene,  
28 polyethylene, polymethyl methacrylate, polypropylene or  
29 other co-polymers of these materials. This exoskeleton  
30 will be typically 1.0mm thick but other thicknesses in  
31 the range 0.5mm to 3mm may be used.  
32

1 Figure 30 shows the rigid exoskeleton 2915 affixed to the  
2 layer 251 plus layer 265 assembly. This may be by  
3 adhesive bonding or by incorporating protrusions in the  
4 exoskeleton 2915 which will snap fit into corresponding  
5 apertures in the supporting layer 251. Where the Layer  
6 265 adjoins an access port on the exoskeleton 2915, for  
7 example, at cavity locations 3021, an adhesive layer,  
8 preferably a commercial silicone rubber compound, will  
9 ensure intimate local contact between Layer 265 and  
10 exoskeleton 2915.

11  
12 Figure 31 shows a section 3100 through the assembly 3101  
13 along the line "D" to "D". Depths are exaggerated in this  
14 figure for clarity, but a typical overall height of the  
15 exoskeleton is 1mm. This cross section shows that  
16 cavities 266 are raised to the height of the exoskeleton,  
17 cavities 269 are raised to a lesser extent (typically  
18 0.5mm) and the channel 267 has a low profile (typically  
19 50 to 200um deep). A conductive strip 253 (typically 20  
20 to 50um thick) is shown entering a cavity 256. Sealing  
21 plugs 3124 are shown at the access port locations. These  
22 sealing plugs will comprise compliant polymer, preferably  
23 an elastomer such as polyurethane or silicone rubber.  
24 These plugs will incorporate a feature allowing removal  
25 and replacement by a simple hand tool or, for continuous  
26 unattended operation, allow automated removal and  
27 replacement. Note also feature 3123 which is a tapered  
28 section of cavity forming a smooth transition between the  
29 cavity 266 and the channel 267.

30  
31 Figure 32 shows a method of loading liquid electrolyte  
32 (for example 2mM Tris, 2mM Acetate, 0.5mM EDTA) by  
33 accessing a probe 3225 into an end cavity. Locations 3226

1 may be vented and sealed (plugs 3124) as part of the  
2 filling process. Note that the micro-scale of the  
3 penetration points will allow surface tension to prevent  
4 unwarranted leakage while the sealing caps are applied.

5  
6 Figure 33 shows a method of pre-loading a column of gel  
7 3328 at the point of manufacture using a loading probe  
8 3327. The gel is loaded as a pre-determined dispensed  
9 volume from the elution cavity end of the test segment.  
10 The gel is preloaded with a fluorescing marker dye.

11  
12 The test segment has now been pre-loaded ready for use,  
13 and will be shipped in this condition to the point of  
14 use. The only "wet chemistry" at the point of use is to  
15 load the test sample for analysis.

16  
17 Figure 34 shows a loading probe 3429 penetrating through  
18 the top loading port of the exoskeleton at the point of  
19 use. The corresponding cap 3124 may be discarded or  
20 replaced depending on whether the tape is required to be  
21 archived after use. The test sample 3430 will be prepared  
22 in a solution which is denser than the surrounding  
23 electrolyte. In the tape cavity, for example, a solution  
24 of sucrose will ensure that the test sample will flow  
25 under gravity into the tapered channel and gather right  
26 at the top of the gel column.

27  
28 The exoskeleton incorporates access ports which can be  
29 oriented longitudinally (e.g. port no. 3431) or  
30 perpendicularly (e.g. port no. 3432). Optionally port  
31 3432 can be used to vent any unwanted build up of gas in  
32 the lower cavity.

33



1 These fabrication methods can create features which  
2 provide a wide range of processing options at the point  
3 of use.

4  
5 With reference to Figure 35, the automated processing has  
6 the steps of transporting the tape and selecting an area  
7 for processing 351, piercing the apparatus with a probe  
8 or probing the apparatus 352, and performing microfluidic  
9 processing 353 at the selected area, then repeating 354  
10 the above steps until processing of the reel of tape is  
11 complete.

12  
13 During these steps the fabricated apparatus with its  
14 optional preloaded processing materials may be deformed  
15 in order to cause dynamic processing. The apparatus may  
16 be deformed by bending, flexing, folding, twisting,  
17 conforming to a rigid surface, mechanical deformation,  
18 deformation by applying a sound pressure, deformation by  
19 applying a liquid pressure, and deformation by applying a  
20 gas pressure. Optionally the deformation can result in  
21 the bringing of a part of the apparatus back into contact  
22 with another part of itself or with another apparatus.  
23 The deformation may move part of the apparatus into a  
24 position for processing, including being in contact with  
25 a processing tool. The deformation of the apparatus  
26 results in dynamic processing that includes pumping,  
27 filling, pouring, pressurising, mixing, dispensing,  
28 aspirating, separating, combining, heating and cooling.

29  
30 Apparatuses that include impermeable membranes facilitate  
31 further novel processing methods that involve the  
32 impermeable membrane. The membrane may be pierced by one  
33 or more probes. These probes may be pipettes.

1 Conducting probes that have pierced the membrane may  
2 provide an electrical potential, and used for passing an  
3 electric current through the conducting probe into a  
4 conducting medium.

5

6 Optionally a grid of probes are mounted on a discrete  
7 carrier or a continuous carrier that can be indexed or  
8 replaced, such that another set of probes can be used  
9 after the first set has worn out.

10

11 The grid of probes may be configured such that each probe  
12 is separately addressable and each probe may have a  
13 separate voltage applied in order to progressively move  
14 the processing material through processing elements, such  
15 as indented troughs and permeation layers in the  
16 apparatus, after the grid of probes has penetrated or  
17 contacted a corresponding grid of impermeable membranes.  
18 This arrangement can be used to move process materials  
19 through permeation layers for molecular separation. The  
20 controlled and progressive switching of voltages on the  
21 grid of probes can be used to split processing material  
22 into more than one separate processing path through more  
23 than one separate processing elements. These split  
24 process materials may be further combined or different  
25 process materials may be combined at the junctions of  
26 paths through the apparatus. In this way, the grid of  
27 electrical probes can be configured to apply voltages  
28 that cause a multi-dimensional separation of molecules,  
29 e.g. polypeptide or protein molecules.

30

31 If the probes are pipettes, processing materials may be  
32 introduced into the apparatus through the impermeable  
33 membranes that have been penetrated or processing

1 materials removed from within the apparatus. An array of  
2 pipettes compatible with 96, 192, 384, 1536 or 3456 well  
3 assay plates can be matched to an array of commensurately  
4 spaced impermeable membranes for penetration by the array  
5 of pipettes. Probes that penetrate or touch the surface  
6 of a membrane can cause processing to be performed, such  
7 as pumping, filling, pouring, pressurising, mixing,  
8 dispensing, aspirating, separating, combining, heating,  
9 cooling, movement by electrokinesis, movement by  
10 electrokinesis, movement by the molecular entrapment  
11 method of molecular tweezers, acoustic tweezers and bio-  
12 molecular motor principles.

13

14 An apparatus in the form of a tape may be transported  
15 through processing equipment and handling equipment by  
16 friction of, for example, rollers in contact with the  
17 apparatus or by pinions inserted into indents or  
18 perforations in the apparatus in a similar manner to the  
19 handling of photographic or cine film. Alternative  
20 methods of moving the tape include sliding drawers and  
21 walking beams. Moving the apparatus with electromagnetic  
22 fields and induction within the apparatus or moving using  
23 air or fluid pressure applied to the apparatus are also  
24 possible.

25

26 The position of the apparatus in response to movement is  
27 detected by measurement of indexing patterns. After  
28 movement dynamic processing can be performed and then  
29 further repeated movement and dynamic processing steps  
30 can be performed in a continuous fashion as the  
31 continuous tape is indexed through the processing  
32 equipment.

33

1 In conclusion, we present the advantages of the present  
2 invention.

3  
4 A significant and long-established traditional art for  
5 some of the kinds of bio-molecular separation described  
6 herein is commonly referred to as "slab gel  
7 electrophoresis". The demands in material usage, process  
8 time, operator time and workspace for this process are  
9 recognised by those with even minor experience of this  
10 art. The procedure commonly employs manual preparation of  
11 gels involving mixing, heating and casting steps.  
12 Although the method can now employ pre-cast gels to  
13 provide some degree of improvement, the overall process  
14 remains manually intensive and inefficient.

15  
16 In contrast, the present invention offers significant  
17 advantages, by miniaturising all the elements of this  
18 traditional process and eliminating many of the material  
19 preparation and manual processing tasks.

20  
21 While the traditional processes remain in common use, new  
22 art is emerging which includes miniaturised bio-analysis  
23 systems employing chip-scale technology, micro-fluidics,  
24 and semiconductor fabrication techniques.

25  
26 The present invention provides advantages over both  
27 traditional and emerging techniques.

28  
29 The present invention provides very significant savings  
30 in materials, time and workspace over traditional gel  
31 electrophoresis methods.

32

1 The present invention provides an adaptable platform for  
2 a very wide range of bio-analysis processes (not just gel  
3 electrophoresis) and employs geometric patterning,  
4 tooling methods and fabrication methods which are much  
5 less complex than other emerging micro-fluidic or chip  
6 scale techniques. This allows rapid and cost effective  
7 production of multiple versions of tape to match the  
8 range of applications anticipated.

9

10 The present invention allows bio-sample processing in a  
11 range from one single simple test up to highly parallel  
12 and multiple complex tests in an uninterrupted continuous  
13 serial or parallel mode. The former is attractive to  
14 small research laboratories, many quality control  
15 laboratories, and point of care clinics. The latter is  
16 attractive to high throughput processing laboratories. A  
17 combination of these processing methods is attractive to  
18 public health hospitals and clinics whose demand can  
19 fluctuate significantly. This range of capability is  
20 provided in one single effective and efficient platform  
21 regardless of usage patterns.

22

23 The present invention configures processing elements on a  
24 highly flexible substrate and enables a versatile range  
25 of substrate indexing patterns and transport methods to  
26 be utilised as described.

27

28 Additionally, these transport methods provide the  
29 advantage of allowing the use of non complex, compact,  
30 low cost optical scanning means by the embodiment of a  
31 fixed position transverse optical line-scanning system  
32 whose focal plane is along a line across the width of the

1 substrate. The scanning function is provided by the  
2 (already provided) indexing motion of the substrate.

3  
4 This highly flexible substrate also enables the other  
5 described features and advantages which result from  
6 bending, folding, twisting, flexing and deforming its  
7 geometry.

8  
9 The substrate flexibility also allows it to be penetrable  
10 by probes for the purposes of processing material  
11 delivery or removal, electrical connection and process  
12 tooling introduction.

13  
14 Additionally this flexible substrate is suitable for  
15 affixing a secondary impermeable membrane which is also  
16 readily penetrable by suitable probes for the purposes of  
17 processing material delivery or removal, electrical  
18 connection, process tooling introduction.

19  
20 The penetrable substrate and penetrable membrane provides  
21 a processing system which can be fully enclosed and which  
22 can provide some processing materials pre-loaded within  
23 the system. This minimises preparation, avoids spillage,  
24 avoids the need for cleaning or flushing procedures and  
25 simplifies waste disposal.

26  
27 Alternatively, a stereo-lithographic method is described  
28 to fabricate the substrate and the impermeable membrane  
29 in one homogenous material with the advantage that this  
30 simplifies the means of construction.

31  
32 Alternatively, a selective laser sintering method is  
33 described to fabricate the substrate and the impermeable

1 membrane in a single fabrication process again with the  
2 advantage that this simplifies the means of construction.

3

4 The present invention employs one generic material type  
5 in its construction (polymer) and avoids the significant  
6 use of glass, silicon or metal in its fabrication. This  
7 simplifies the waste disposal methods after bio-  
8 processing is complete.

9

10 The fabrication techniques described provide a wide range  
11 of substrate geometries. These features can be created  
12 by rapid and simple methods of tooling, thus avoiding the  
13 long lead times and complexity of other miniaturised bio-  
14 processing systems.

15

16 The present invention has the advantage that these rapid  
17 and simple fabrication techniques correspond to  
18 processing elements whose dimensional accuracy is less  
19 critical than those of chip scale devices. A  
20 corresponding advantage is that this is achieved without  
21 sacrifice to the overall device size because the device  
22 size, in the current state of the art, is determined by  
23 the practicalities of the size of the sample loading  
24 wells and not by the processing element sizes.

25

26 The present invention can be enhanced by pre-printing  
27 processing materials onto a planar plastic film substrate  
28 using commercially available printing methods and then by  
29 deforming that substrate in a non planar fashion such  
30 that the pre-printed material deforms into a desired  
31 shape or position and such that, for example, a pre-  
32 printed permeation layer can subsequently (after forming  
33 of the substrate) be hydrated into its gelatinous phase.

1 Related printing and forming methods are already  
2 established in the field of foil manufacture for "in-  
3 mould decoration" of plastic injection moulded products  
4 (used for cosmetic effect mainly on consumer electronic  
5 products), but the present invention provides the scope  
6 for adapting these methods into this unconnected field of  
7 application.

8  
9 The flexible substrate is readily available in a range of  
10 polymer materials whose optical properties can be matched  
11 to available commercial optical systems for detection or  
12 imaging of the bio-processing events during system  
13 operation.

14  
15 Further modifications and improvements may be added  
16 without departing from the scope of the invention herein  
17 described.



1 CLAIMS

2

3 1. An apparatus for microfluidic processing  
4 applications, wherein said microfluidic processing  
5 is performed on a selected area of a plurality of  
6 areas each individually selectable on said  
7 apparatus, characterised in that the apparatus is  
8 non-rigid.

9

10 2. An apparatus for mass transport microfluidic  
11 processing applications, characterised in that the  
12 apparatus is non-rigid.

13

14 3. The apparatus of any previous Claim, wherein said  
15 apparatus is a tape.

16

17 4. The apparatus of any previous Claim, wherein said  
18 apparatus comprises a polymer film.

19

20 5. The apparatus of any previous Claim, wherein said  
21 apparatus comprises processing elements for  
22 microfluidic processing.

23

24 6. The apparatus of Claim 5, wherein said processing  
25 elements comprise indents of said apparatus.

26

27 7. The apparatus of any of Claims 5 to 6, wherein said  
28 processing elements comprise cavities embedded  
29 within said apparatus.

30

31 8. The apparatus of any of Claims 5 to 7, wherein said  
32 processing elements comprise processing materials in  
33 intimate contact with the surface of said apparatus.

- 1
- 2 9. The apparatus of any of Claims 5 to 8, wherein said
- 3 processing elements comprise processing materials
- 4 embedded within said apparatus.
- 5
- 6 10. The apparatus of any of Claims 5 to 9, wherein said
- 7 processing elements comprise opaque, translucent or
- 8 coloured materials for providing optical isolation
- 9 between elements or providing indexing marks.
- 10
- 11 11. The apparatus of any previous Claim, wherein an
- 12 element of said apparatus is transparent.
- 13
- 14 12. The apparatus of any previous Claim, wherein said
- 15 apparatus is penetrable.
- 16
- 17 13. The apparatus of Claim 12, wherein said apparatus is
- 18 self sealing during penetration.
- 19
- 20 14. The apparatus of Claims 12 to 13, wherein said
- 21 apparatus is self sealing after penetration.
- 22
- 23 15. The apparatus of any previous Claim, wherein said
- 24 apparatus further comprises an impermeable membrane.
- 25
- 26 16. The apparatus of Claim 15, wherein said impermeable
- 27 membrane is affixed in intimate contact with parts
- 28 of the surface of said apparatus.
- 29
- 30 17. The apparatus of any of Claims 15 to 16, wherein
- 31 said impermeable membrane is arranged as discrete
- 32 areas of impermeable membrane in intimate contact
- 33 with parts of the surface of said apparatus.

- 1
- 2 18. The apparatus of any of Claims 15 to 17, wherein
- 3 said impermeable membrane is penetrable.
- 4
- 5 19. The apparatus of any of Claims 15 to 18, wherein
- 6 said impermeable membrane is self sealing during
- 7 penetration.
- 8
- 9 20. The apparatus of any Claims 15 to 19, wherein said
- 10 impermeable membrane is self sealing after
- 11 penetration.
- 12
- 13 21. The apparatus of any Claims 15 to 20, wherein said
- 14 impermeable membrane is re-sealed by a capping
- 15 element after penetration.
- 16
- 17 22. The apparatus of any Claims 15 to 21, wherein said
- 18 impermeable membrane is supported by support
- 19 structures.
- 20
- 21 23. The apparatus of any previous Claim, wherein said
- 22 apparatus further comprises a non-rigid member.
- 23
- 24 24. The apparatus of Claim 23, wherein said non-rigid
- 25 member is affixed in intimate contact with parts of
- 26 the surface of said apparatus.
- 27
- 28 25. The apparatus of any of Claims 23 to 24, wherein
- 29 said non-rigid member is arranged as discrete areas
- 30 of non-rigid member in intimate contact with parts
- 31 of the surface of said apparatus.
- 32

- 1 26. The apparatus of any of Claims 23 to 24, wherein  
2 said non-rigid member is penetrable.  
3
- 4 27. The apparatus of any of Claims 23 to 26, wherein  
5 said non-rigid member is self sealing during  
6 penetration.  
7
- 8 28. The apparatus of any of Claims 23 to 27, wherein  
9 said non-rigid member is self sealing after  
10 penetration.  
11
- 12 29. The apparatus of any of Claims 23 to 28, wherein  
13 said non-rigid member is re-sealed by a capping  
14 element after penetration.  
15
- 16 30. The apparatus of any of Claims 23 to 29, wherein  
17 said non-rigid member is supported by support  
18 structures.  
19
- 20 31. A method of fabrication of an apparatus for mass  
21 transport microfluidic processing applications  
22 comprising the step of forming an apparatus that is  
23 non-rigid.  
24
- 25 32. A method of fabrication of an apparatus for mass  
26 transport microfluidic processing applications  
27 comprising the step of fabricating a tape.  
28
- 29 33. The method according to any of Claims 31 to 32,  
30 wherein said step of forming said apparatus  
31 comprises the step of high pressure plastic film  
32 forming with said high pressure acting on said  
33 apparatus.

- 1  
2 34. The method of Claim 33, wherein said step of high  
3 pressure plastic film forming is arranged with the  
4 high pressure acting on a compliant membrane, which  
5 is part of the forming tool in contact with said  
6 apparatus.  
7  
8 35. The method of any of Claims 31 to 34, wherein said  
9 step of fabricating said apparatus further comprises  
10 the step of preloading processing materials onto  
11 said apparatus before fabrication.  
12  
13 36. The method of any of Claims 31 to 34, wherein said  
14 step of fabricating said apparatus further comprises  
15 the step of loading processing materials onto said  
16 apparatus during fabrication.  
17  
18 37. The method of Claim 36, wherein said step of  
19 preloading or loading during fabrication of said  
20 apparatus comprises the step of depositing  
21 processing materials onto a carrier.  
22  
23 38. The method of Claim 36, wherein said step of  
24 preloading or loading during fabrication of said  
25 apparatus comprises the step of depositing  
26 processing material onto a non-rigid member.  
27  
28 39. The method of any of Claims 36 to 38, wherein said  
29 deposited processing material comprises permeation  
30 layers.  
31

- 1 40. The method of any of Claims 36 to 39, wherein said  
2 deposited processing material comprises conductive  
3 material.  
4
- 5 41. The method of any of Claims 36 to 40, wherein said  
6 deposited processing material comprises chemically  
7 or biologically active material.  
8
- 9 42. The method of any of Claims 36 to 41, wherein said  
10 deposited processing material comprises marks for  
11 identity purposes.  
12
- 13 43. The method of any of Claims 36 to 42, wherein said  
14 deposited processing material comprises magnetisable  
15 material.  
16
- 17 44. The method of any of Claims 36 to 43, wherein said  
18 step of depositing comprises printing.  
19
- 20 45. The method of Claim 36, wherein said step of  
21 preloading or loading during fabrication of said  
22 apparatus is performed by a loading process selected  
23 from a list of processes comprising: deposition and  
24 etching, injection into a cavity and injection into  
25 an indentation.  
26
- 27 46. The method of any of Claims 31 to 34, wherein said  
28 method of fabrication of said apparatus further  
29 comprises the steps of depositing patterns on an  
30 apparatus and forming said apparatus, wherein the  
31 localised formation of said processing elements is  
32 responsive to the distortion by said forming of said  
33 deposited pattern.

1

2 47. The method of any of Claims 31 to 34, wherein said  
3 method of fabrication of said apparatus further  
4 comprises the steps of depositing patterns on an  
5 apparatus and localised formation of said apparatus  
6 is responsive to the topography of said deposited  
7 pattern, resulting in the formation of said  
8 processing elements.

9

10 48. The method of any of Claims 46 to 47, wherein said  
11 step of depositing comprises pre-printing.

12

13 49. A method of fabrication of an apparatus for mass  
14 transport microfluidic processing applications,  
15 comprising the step of including an impermeable  
16 membrane as part of said apparatus.

17

18 50. The method of Claim 49, wherein said step of  
19 including an impermeable membrane comprises the step  
20 of affixing an impermeable membrane to a substrate.

21

22 51. The method of any of Claims 49 to 50, wherein said  
23 step of including an impermeable membrane comprises  
24 the step of depositing, overlaying or affixing  
25 discrete areas of impermeable membrane in intimate  
26 contact with parts of the surface of said apparatus.

27

28 52. The method of any of Claims 49 to 51, wherein said  
29 step of including an impermeable membrane comprises  
30 the step of depositing, overlaying or affixing an  
31 impermeable membrane on said apparatus and  
32 selectively removing areas of said impermeable  
33 membrane.

1

2 53. The method of Claim 52 wherein said selected removal  
3 of said impermeable membrane is performed by the  
4 step of cropping.

5

6 54. A method of fabrication of an apparatus for mass  
7 transport microfluidic processing applications,  
8 comprising the step of including a non-rigid member  
9 as part of said apparatus.

10

11 55. The method of Claim 54, wherein said step of  
12 including a non-rigid member comprises the step of  
13 affixing a non-rigid member to a substrate.

14

15 56. The method of any of Claims 54 to 55, wherein said  
16 step of including a non-rigid member comprises the  
17 step of depositing, overlaying or affixing discrete  
18 areas of non-rigid member in intimate contact with  
19 parts of the surface of said apparatus.

20

21 57. The method of any of Claims 54 to 56, wherein said  
22 step of including a non-rigid member comprises the  
23 step of depositing, overlaying or affixing a non-  
24 rigid member on said apparatus and selectively  
25 removing areas of said non-rigid member.

26

27 58. The method of Claim 57, wherein said selected  
28 removal of said non-rigid member is performed by the  
29 step of cropping.

30

31 59. A method of microfluidic processing, comprising the  
32 steps of selecting an area of a plurality of areas  
33 of an apparatus and performing microfluidic



1 processing at said selected area, characterised in  
2 that said apparatus is non-rigid.

3

4 60. The method of Claim 59, wherein said step of  
5 performing microfluidic processing comprises  
6 contacting at least one conducting element that  
7 connects the exterior of said apparatus to the  
8 interior of said apparatus.

9

10 61. The method of Claim 60, further comprising the step  
11 of providing an electrical potential to at least one  
12 conducting element.

13

14 62. The method of any of Claims 59 to 60, further  
15 comprising the step of enabling an electrical  
16 current to pass through said least one conducting  
17 element.

18

19 63. The method of any of Claims 31 to 62, wherein said  
20 apparatus is a tape.

21

22 64. The method of any of Claims 31 to 63, wherein said  
23 microfluidic processing is mass transport  
24 microfluidic processing.

25

26 65. The method of any of Claims 31 to 64, wherein said  
27 microfluidic processing is responsive to the  
28 deformation of said apparatus.

29

30 66. The method of Claim 65, wherein said deformation  
31 comprises deformation by a step selected from a list  
32 of steps comprising: bending, flexing, folding,  
33 twisting, conforming to a rigid surface, mechanical

1 deformation, deformation by applying a sound  
2 pressure, deformation by applying a liquid pressure,  
3 and deformation by applying a gas pressure.  
4

5 67. The method of Claim 66, wherein said gas pressure is  
6 a negative pressure.  
7

8 68. The method of any of Claims 66 to 67, wherein said  
9 deformation may further comprise the step of  
10 bringing part of said apparatus back into contact  
11 with another part of itself.  
12

13 69. The method of any of Claims 66 to 67, wherein said  
14 step of deformation further comprises the step of  
15 bringing a part of said apparatus into contact with  
16 another apparatus.  
17

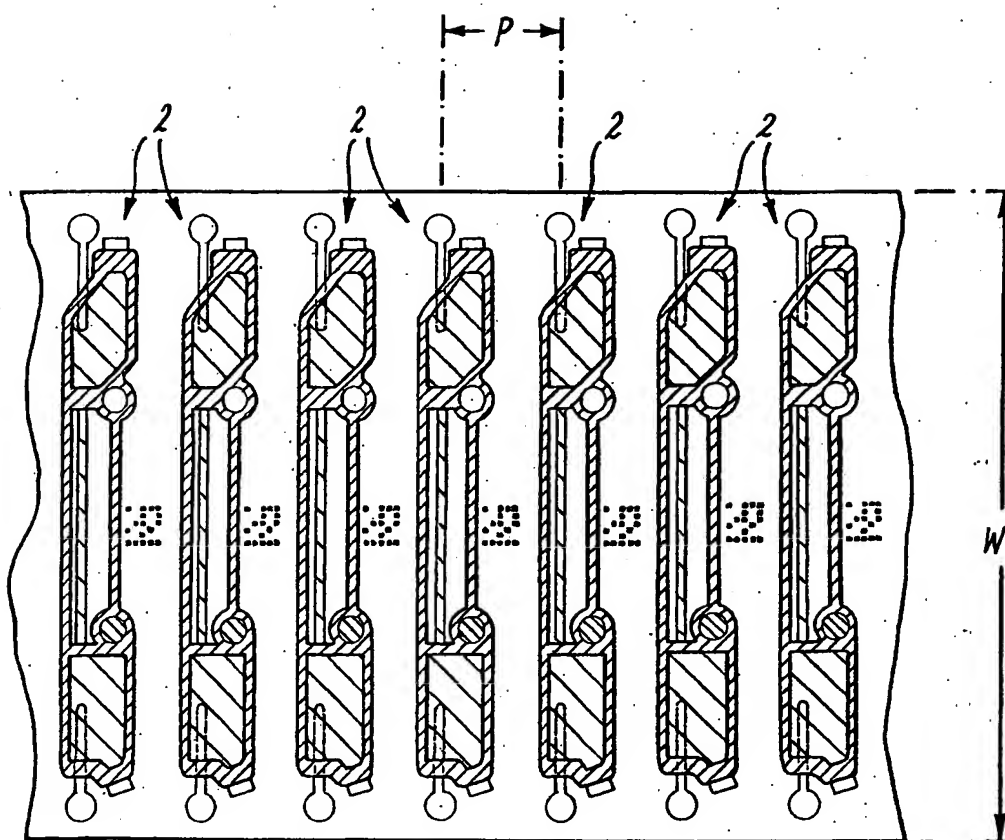
18 70. The method of any of Claims 66 to 67, wherein said  
19 deformation of said apparatus comprises the step of  
20 moving part of said apparatus into a position for  
21 processing of said part of said apparatus.  
22

23 71. The method of Claim 70, wherein said position for  
24 processing is a position with said apparatus in  
25 contact with a processing tool.  
26

27 72. The method of any of Claims 65 to 71, wherein said  
28 microfluidic processing is responsive to said  
29 deformation of said apparatus, said microfluidic  
30 processing being selected from a list comprising  
31 pumping, filling, pouring, pressurising, mixing,  
32 dispensing, aspirating, separating, combining,  
33 heating and cooling.

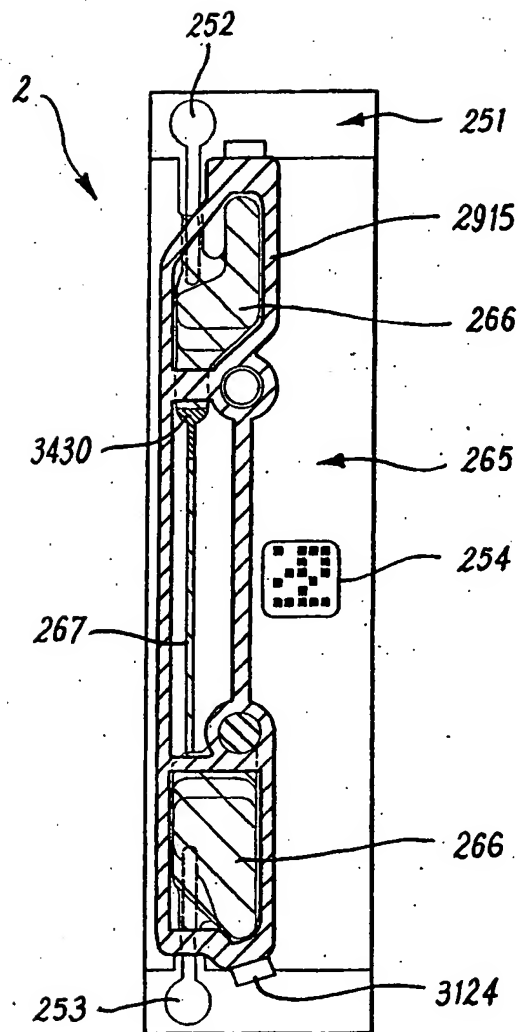
- 1
- 2 73. A method of processing for microfluidic processing
- 3 applications, characterised in that the processing
- 4 comprises the step of piercing an impermeable
- 5 membrane.
- 6
- 7 74. The method of Claim 73, wherein said step of
- 8 piercing an impermeable membrane is performed with
- 9 at least one probe.
- 10
- 11 75. The method of Claim 74, wherein said at least one
- 12 probe comprises at least one pipette.
- 13
- 14 76. The method of Claim 74, wherein said method of
- 15 processing further comprises the step of providing
- 16 an electrical potential to at least one conducting
- 17 probe that has pierced said membrane.
- 18
- 19 77. The method of Claim 74, wherein said step of
- 20 processing further comprises the step of enabling an
- 21 electrical current to pass through at least one
- 22 conducting probe that has pierced said membrane.
- 23
- 24 78. A method of processing for microfluidic processing
- 25 applications, characterised in that the processing
- 26 comprises the step of piercing an apparatus.
- 27
- 28 79. The method of Claim 78, wherein said apparatus is
- 29 self sealing during said step of piercing.
- 30
- 31 80. The method of any of Claims 78 to 79, wherein said
- 32 apparatus is self sealing after said step of
- 33 piercing.

- 1
- 2 81. The method of Claim 78, wherein said apparatus is
- 3 re-sealed by a capping element after penetration.
- 4
- 5 82. The method of any of Claims 78 to 81, wherein said
- 6 step of piercing the apparatus is performed with at
- 7 least one probe.
- 8
- 9 83. The method of Claim 82, wherein said at least one
- 10 probe comprises at least one pipette.
- 11
- 12 84. The method of Claims 82 to 83, wherein said method
- 13 of processing further comprises the step of
- 14 providing an electrical potential to at least one
- 15 conducting probe that has pierced said apparatus.
- 16
- 17 85. The method of Claims 82 to 84, wherein said step of
- 18 processing further comprises the step of enabling an
- 19 electrical current to pass through a conducting
- 20 probe that has pierced said apparatus.

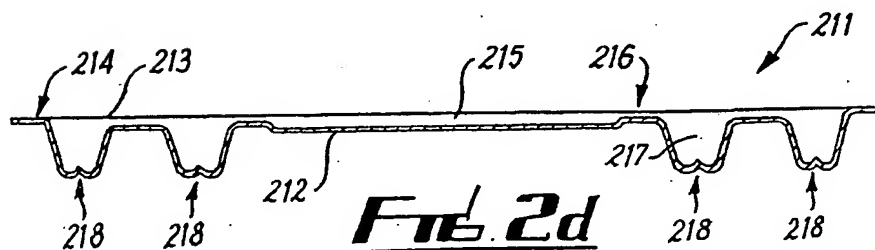
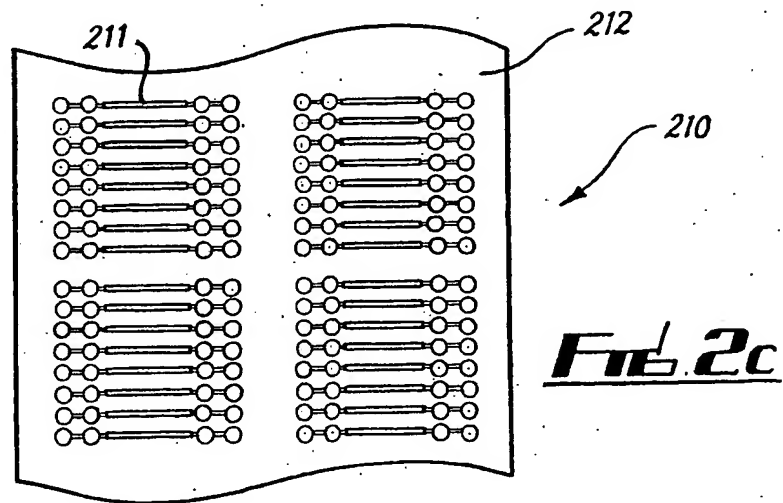
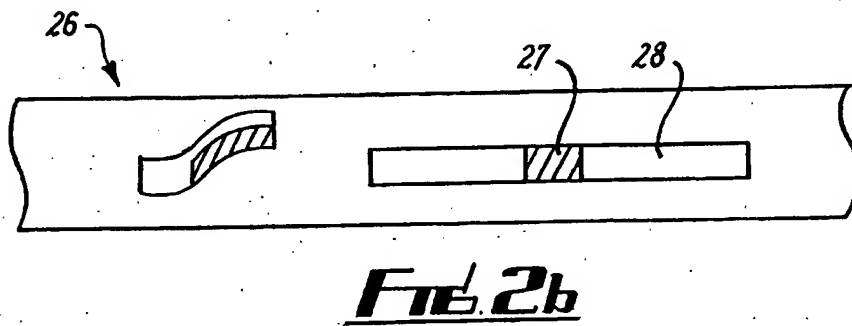
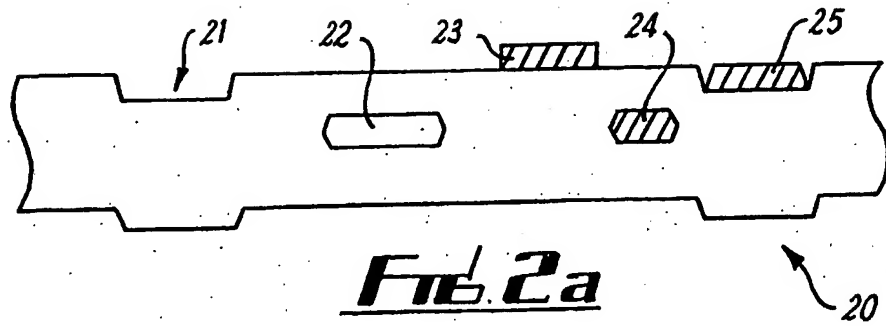


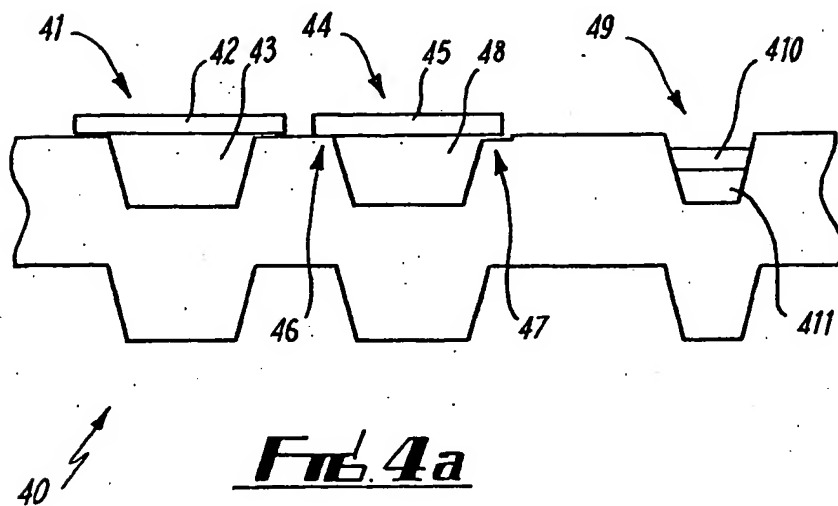
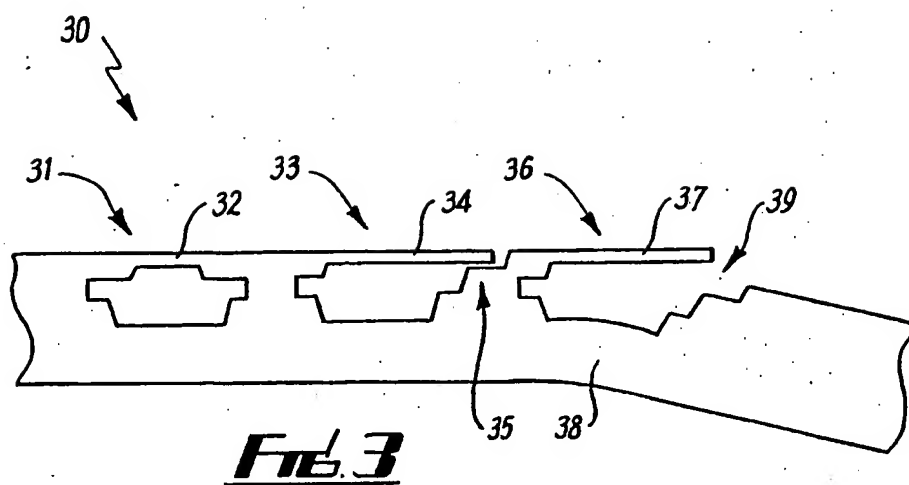
1 ↗

**Fig. 1a**

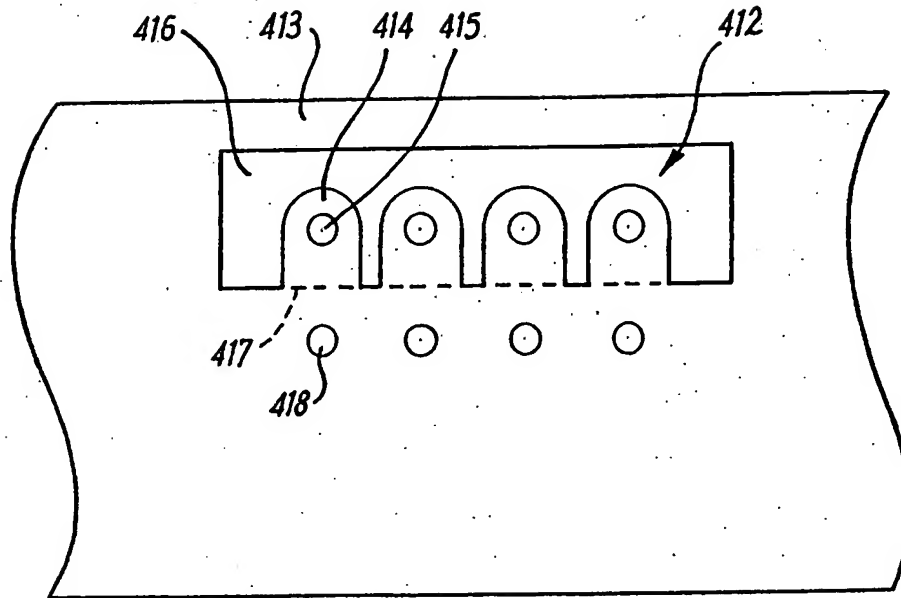


***FIG. 1b***

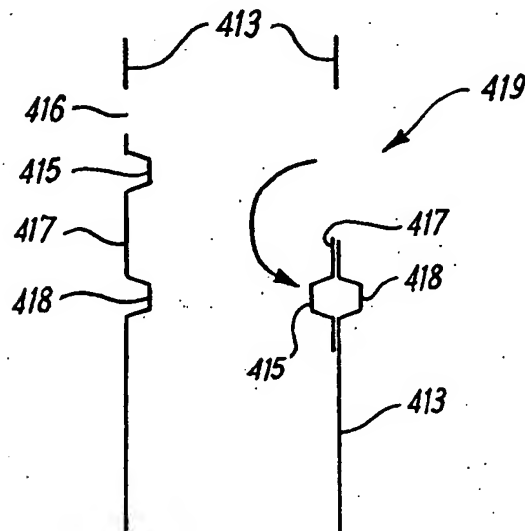




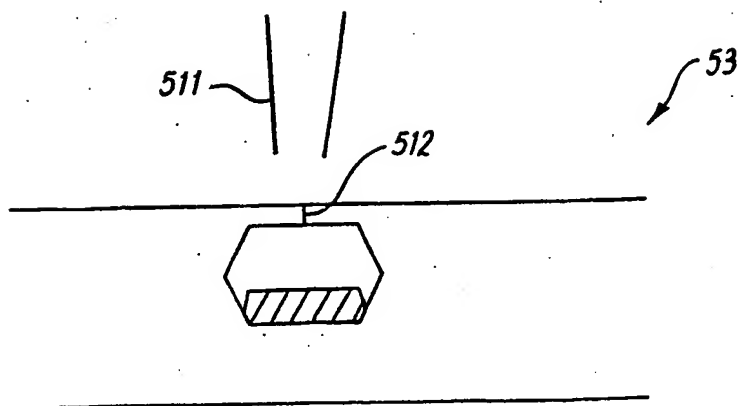
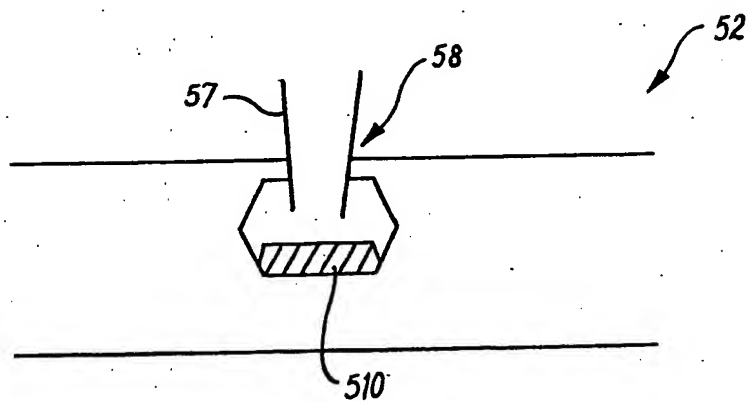
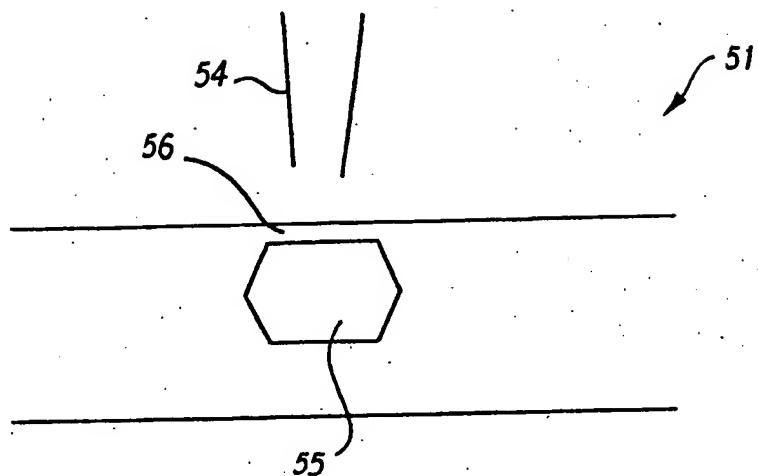




**Fig. 4b**

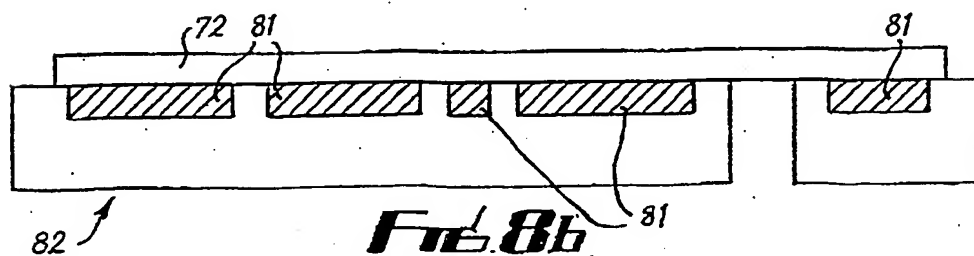
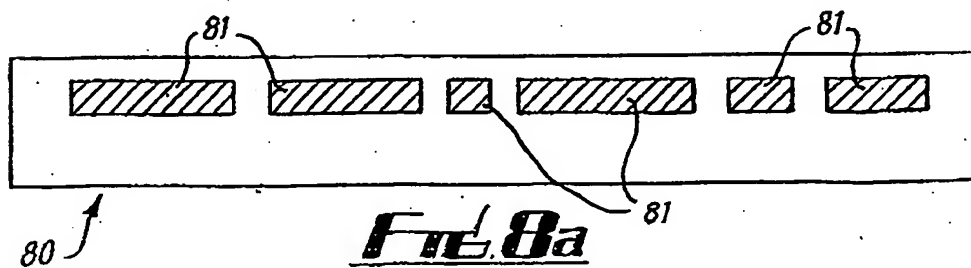
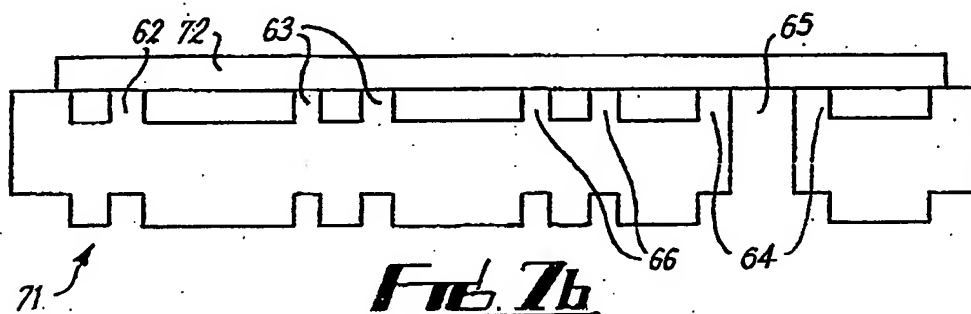
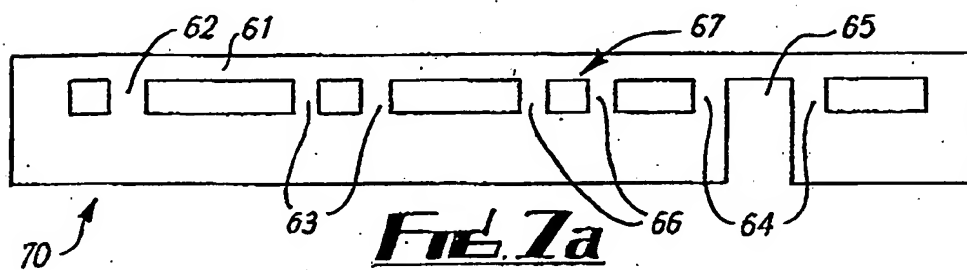
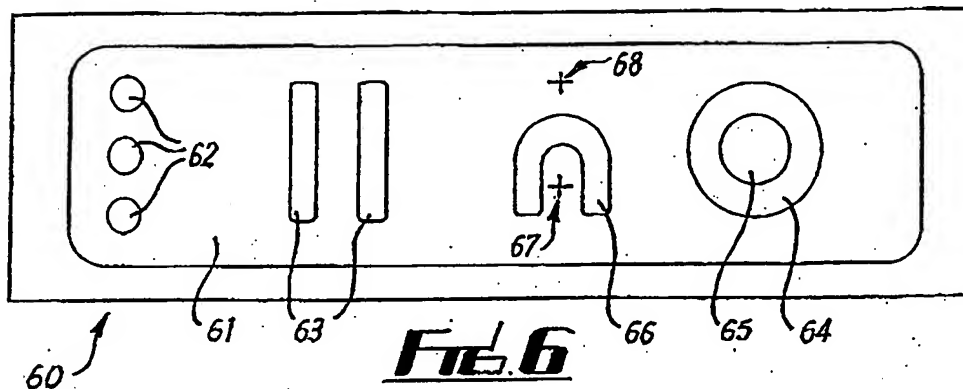


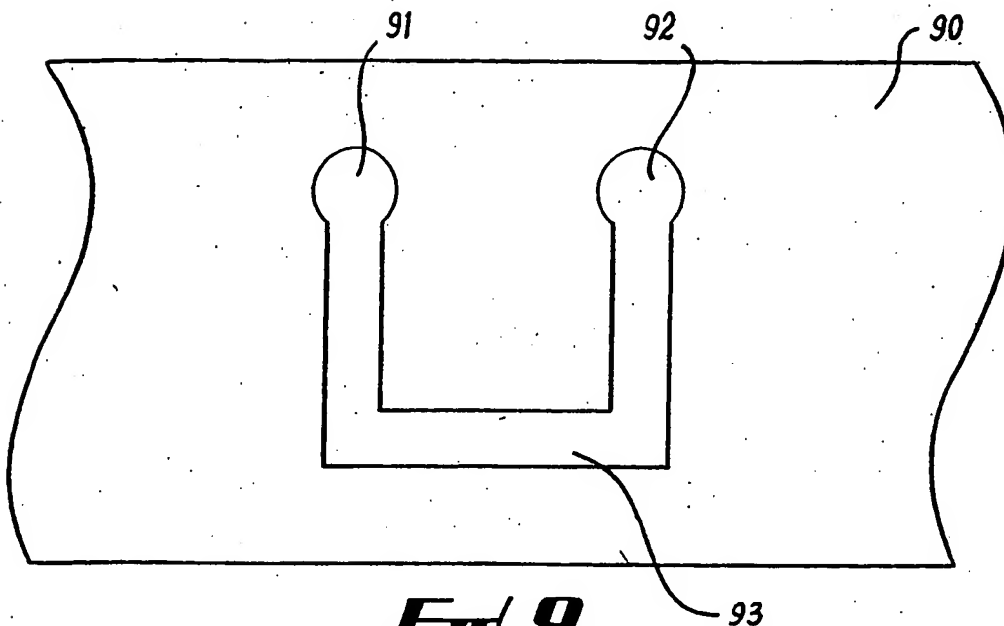
**Fig. 4c**



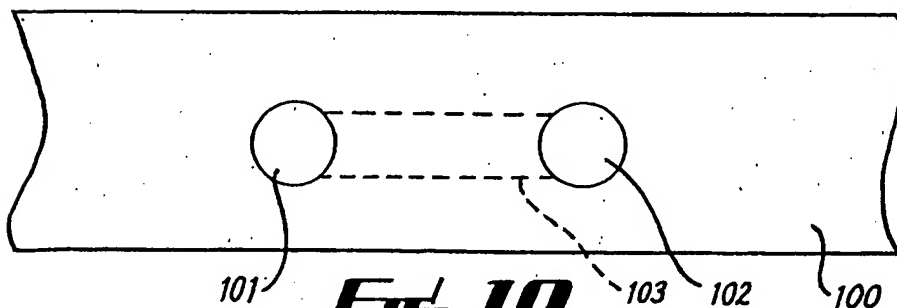
**FIG. 5**

SUBSTITUTE SHEET (RULE 26)

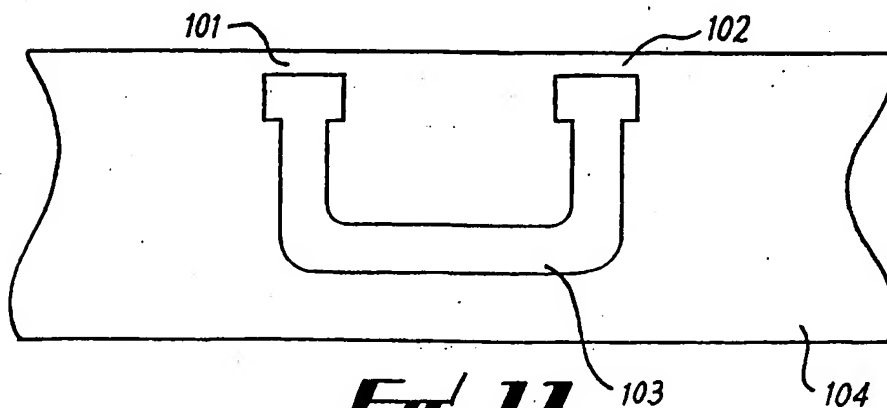




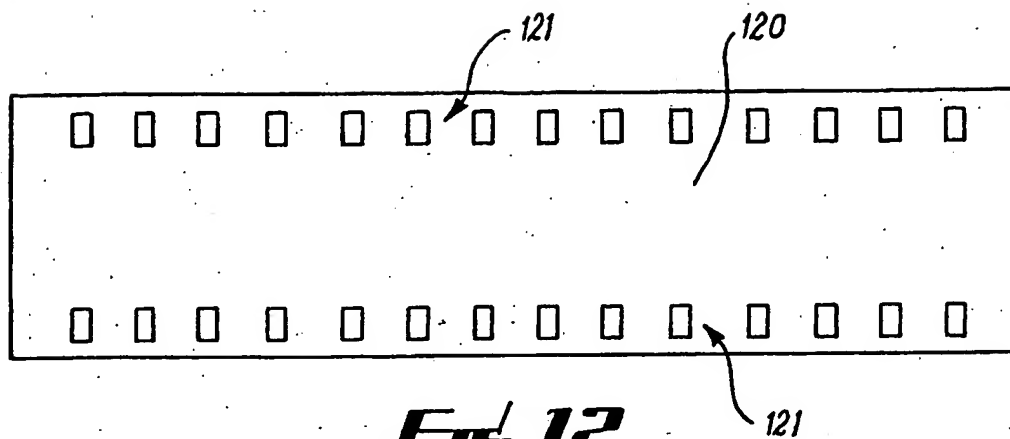
**FIG. 9**



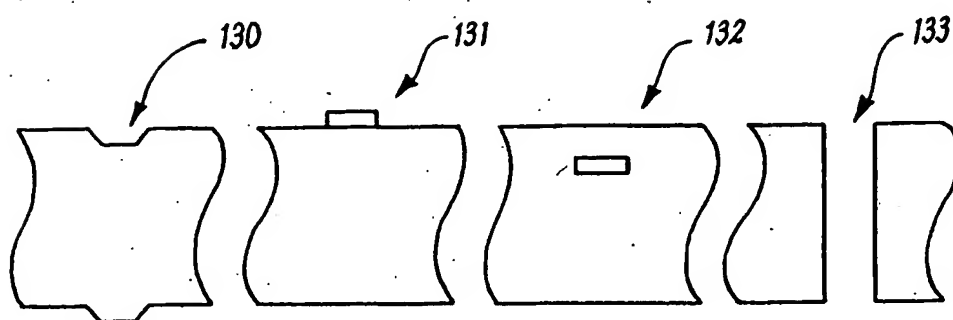
**FIG. 10**



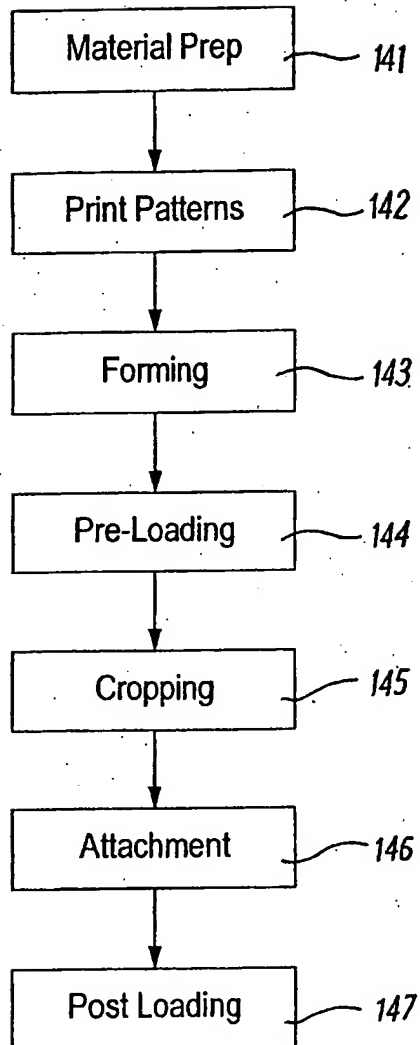
**FIG. 11**



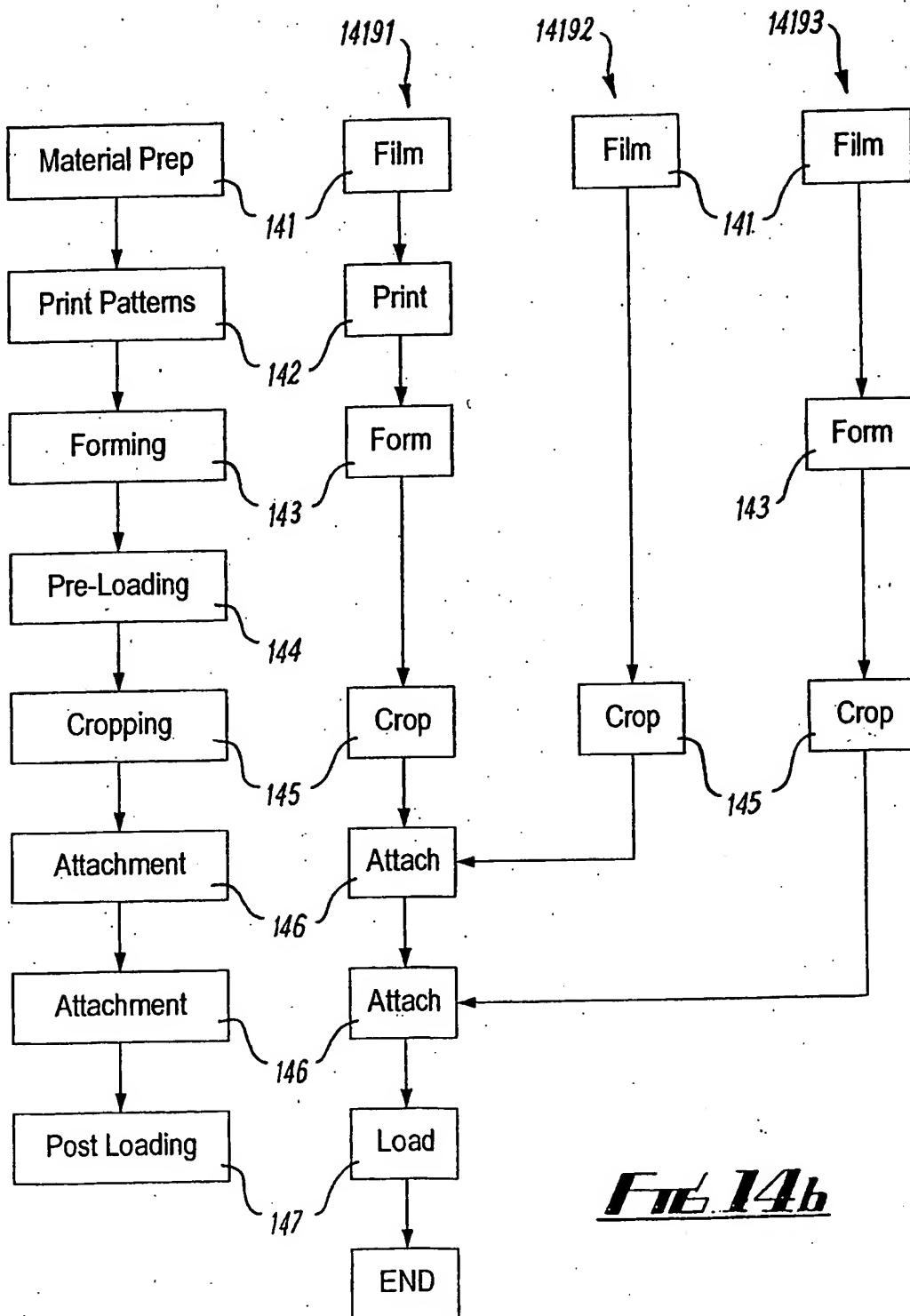
**Fig. 12**

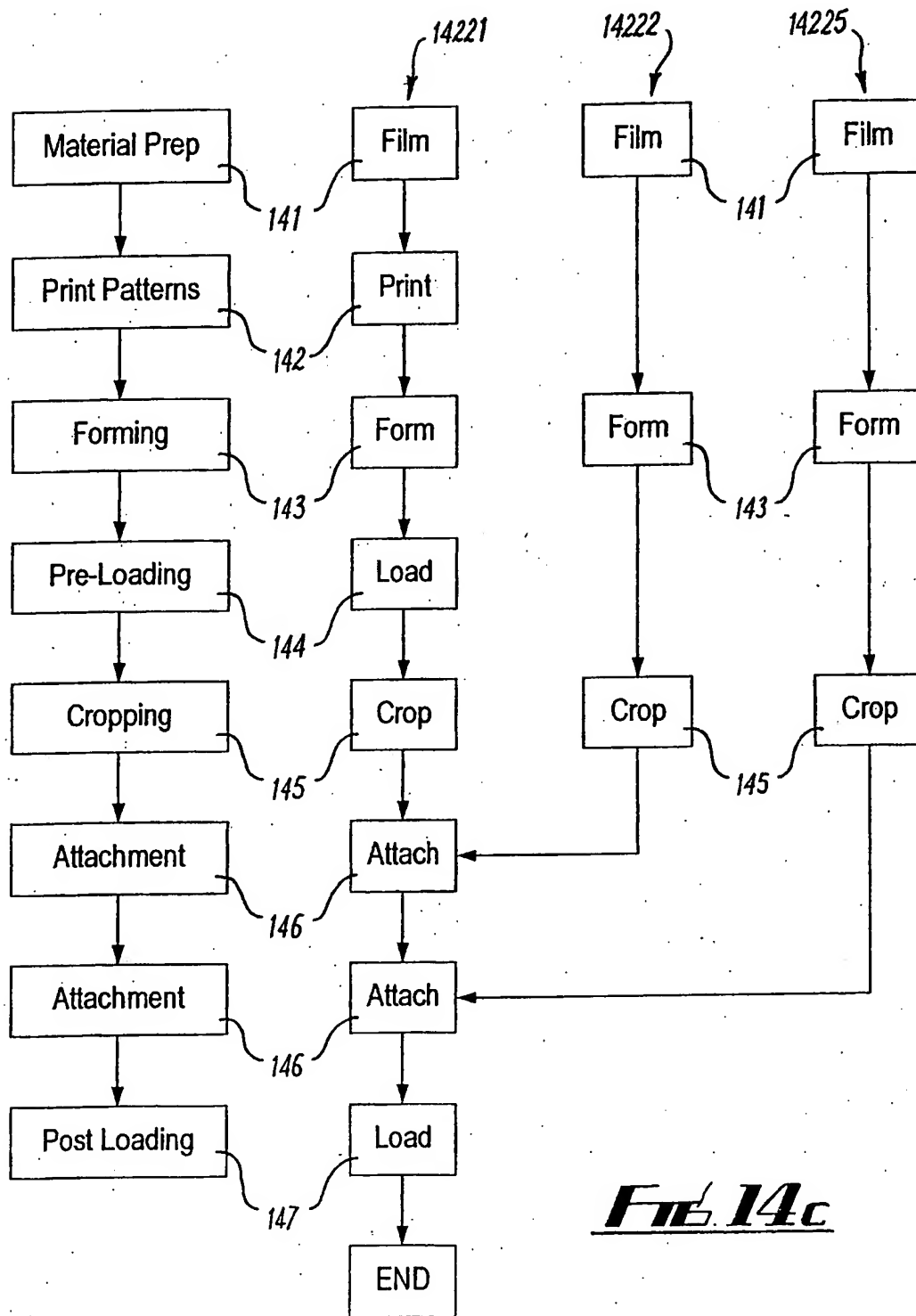


**Fig. 13**

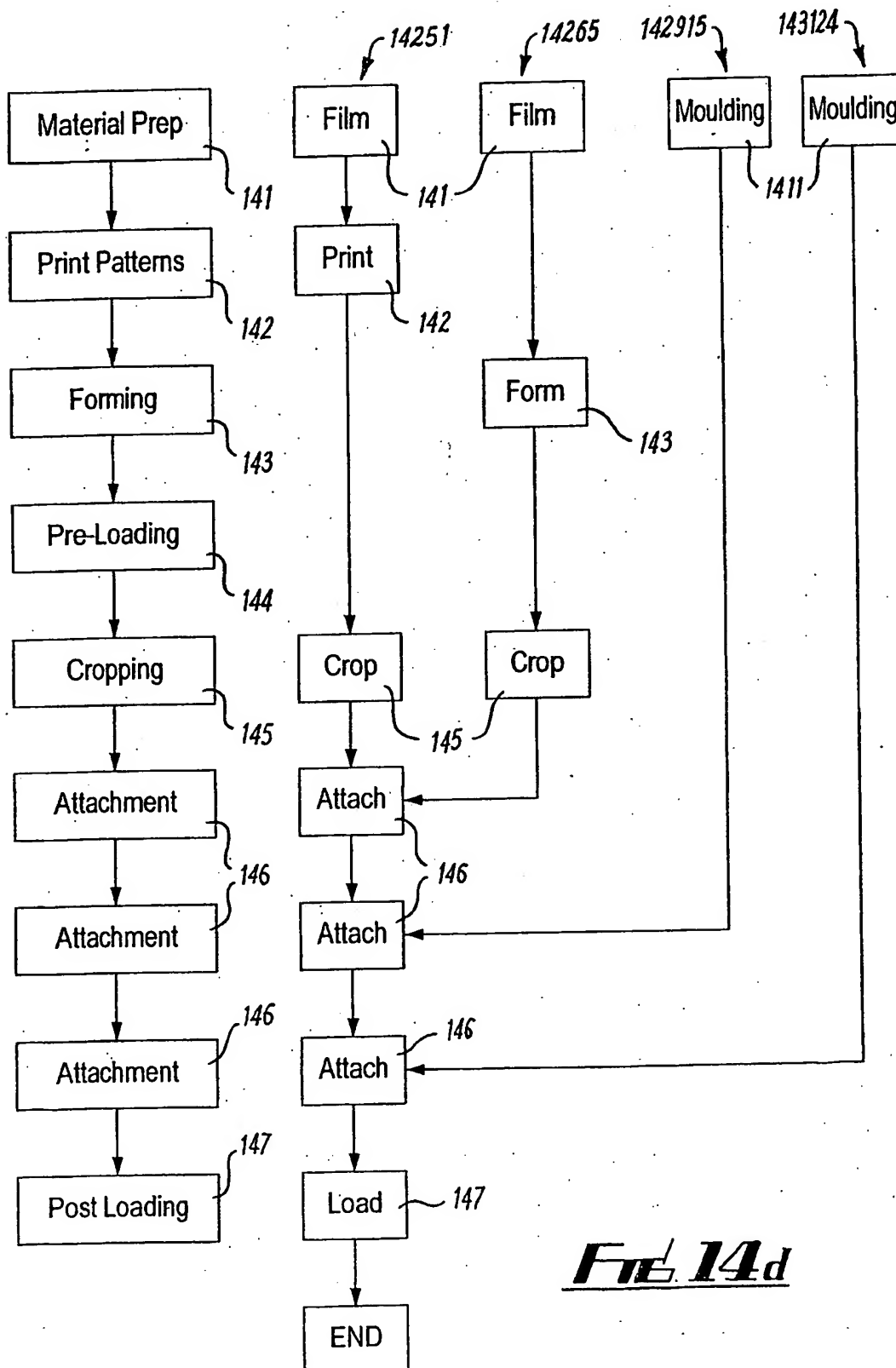


***FIG. 14a***

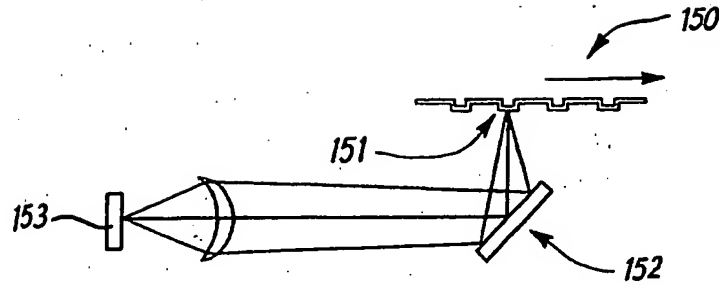


***FIG. 14c***

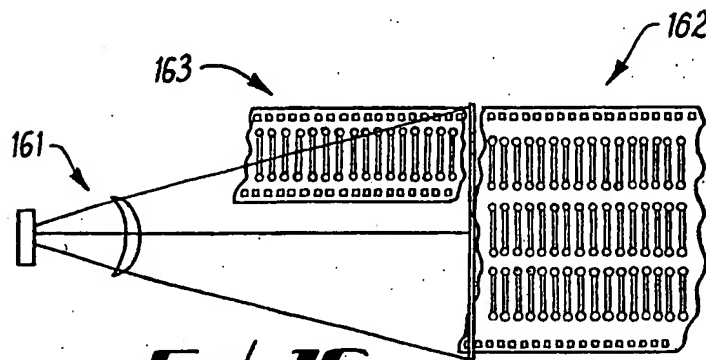


***FIG. 14d***

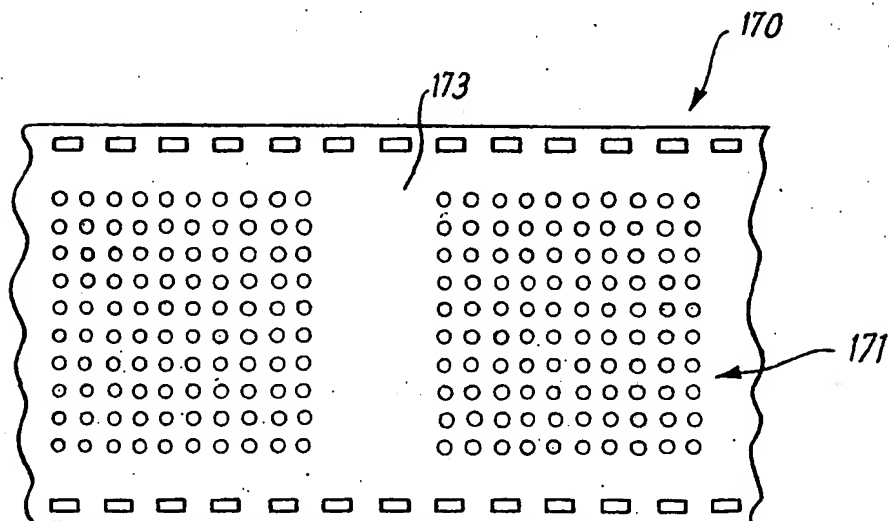
14/21



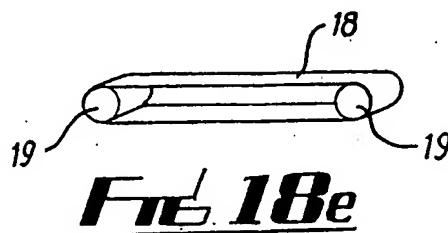
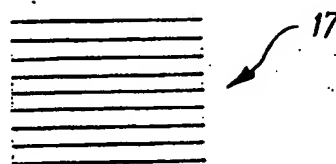
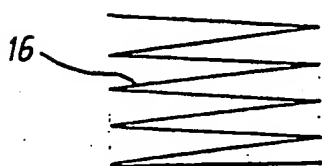
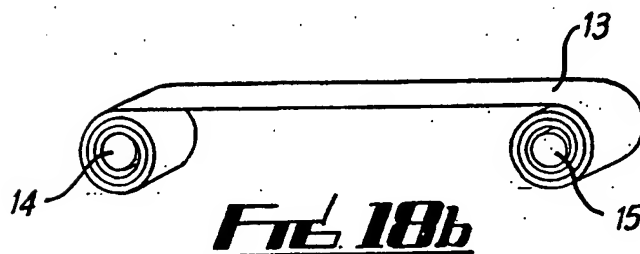
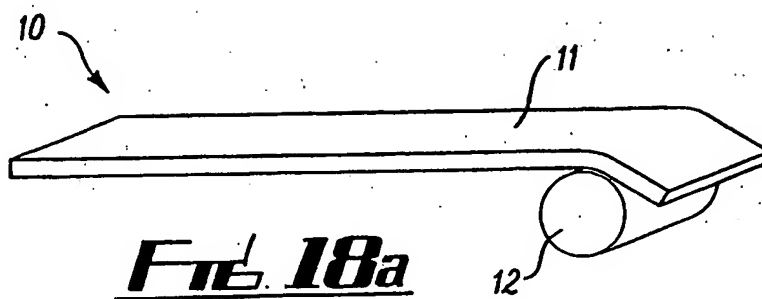
**Fig. 15**

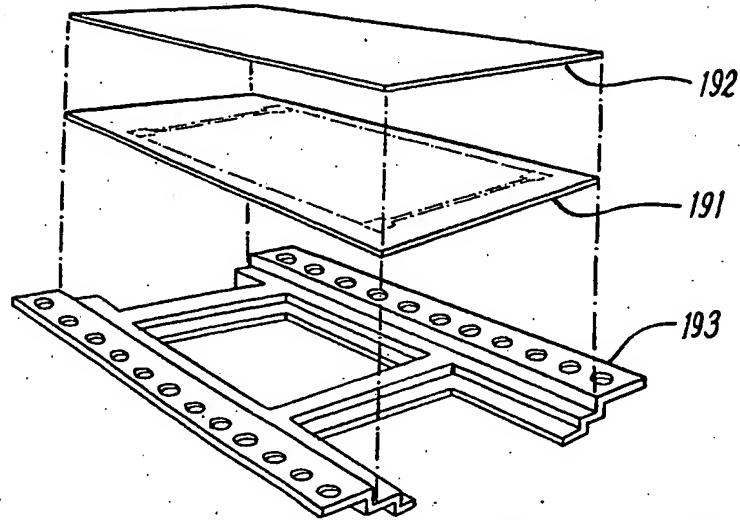


**Fig. 16**

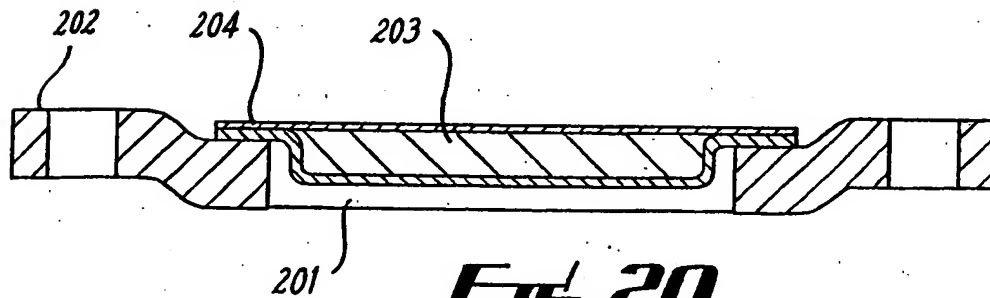


**Fig. 17**

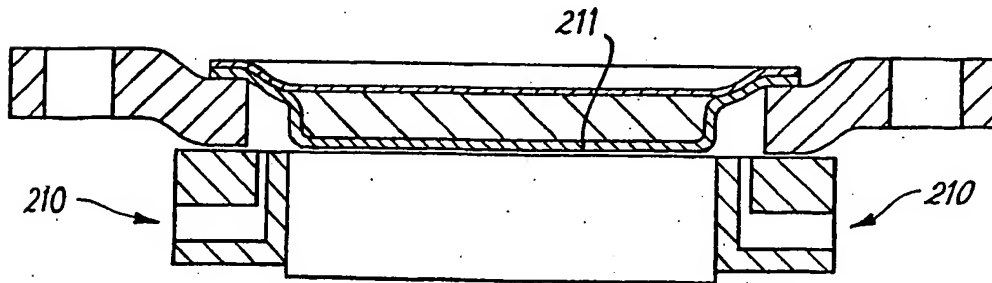




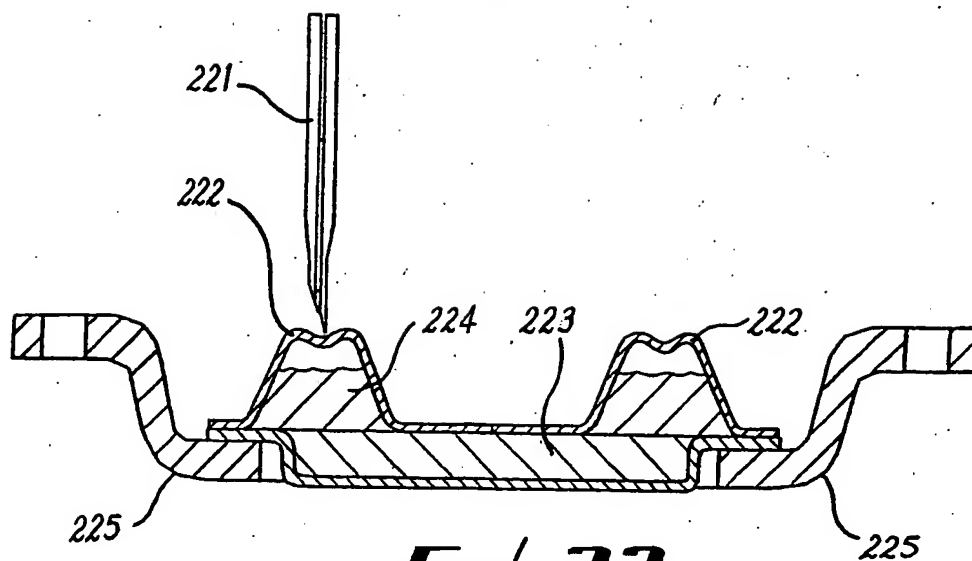
**FIG. 19**



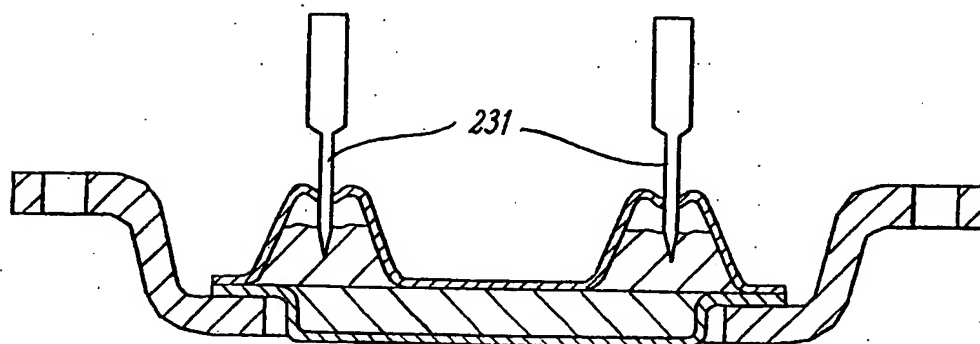
**FIG. 20**



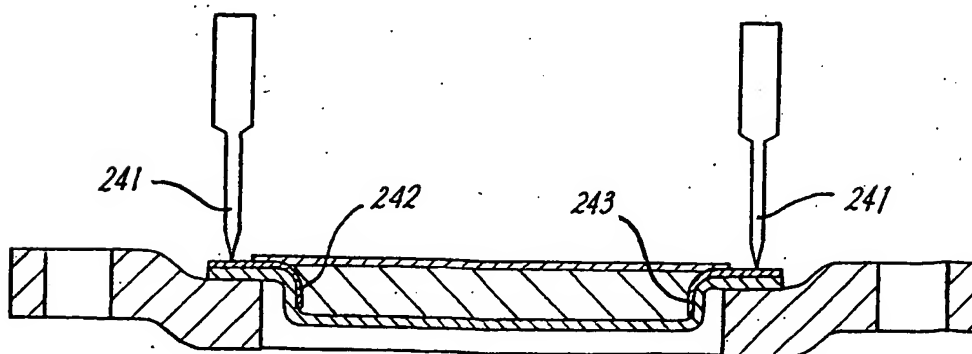
**FIG. 21**



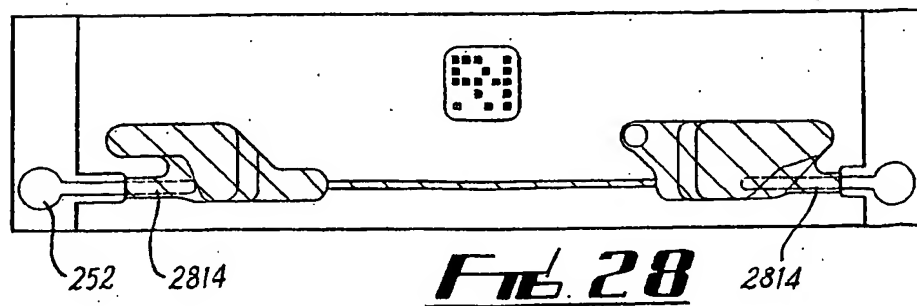
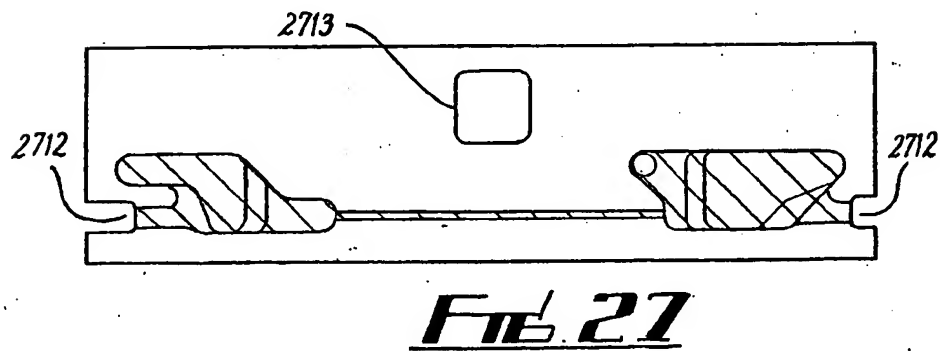
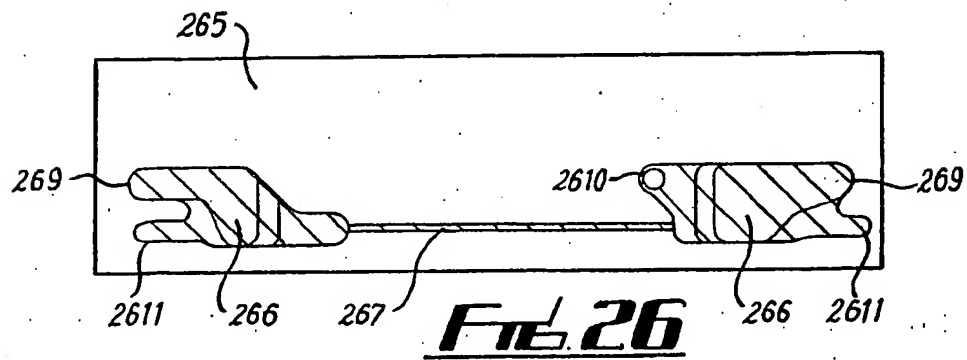
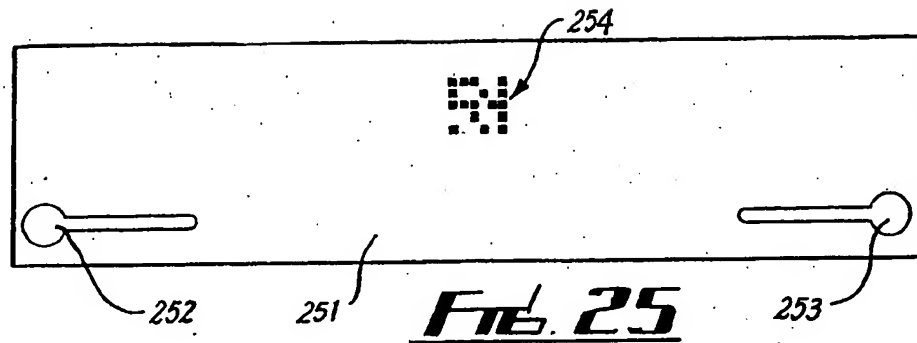
**FIG. 22**

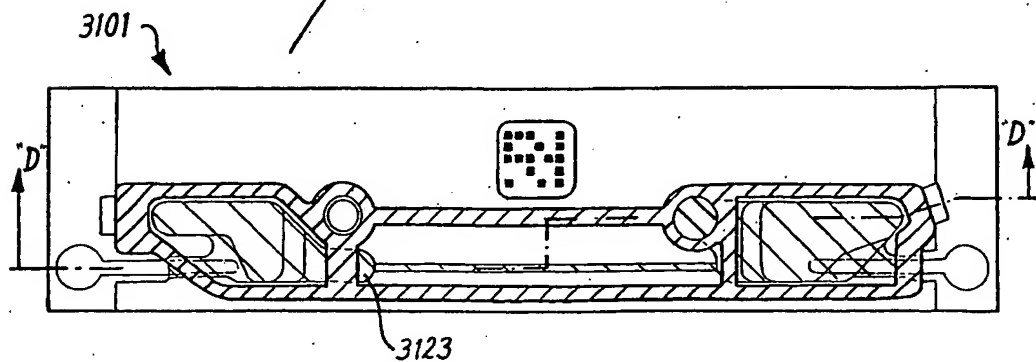
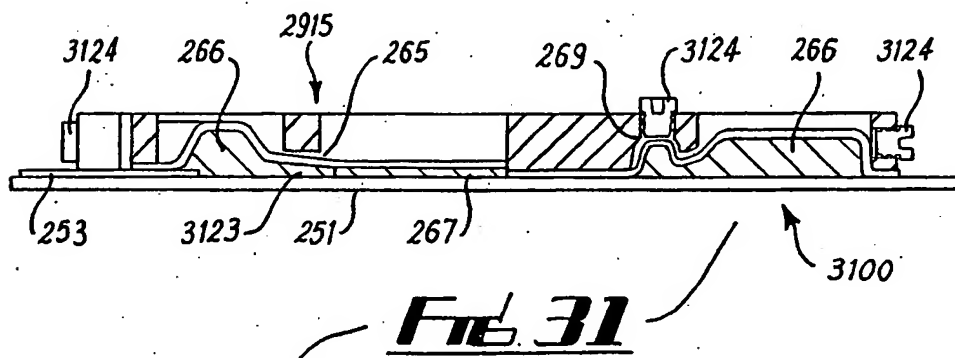
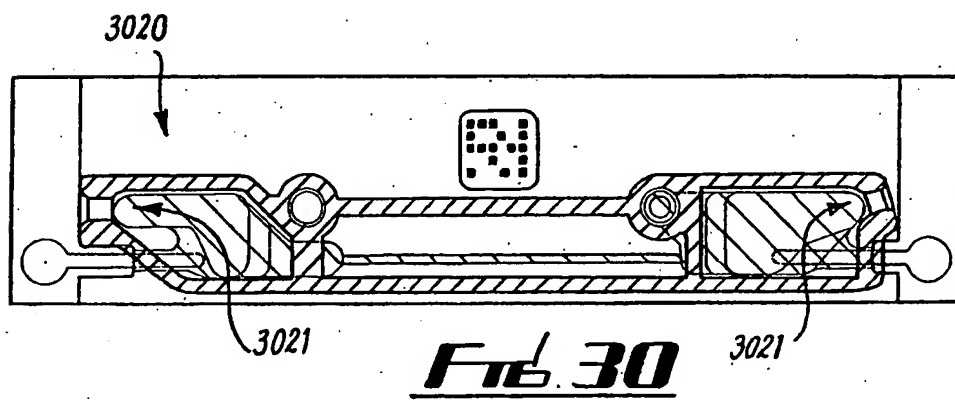
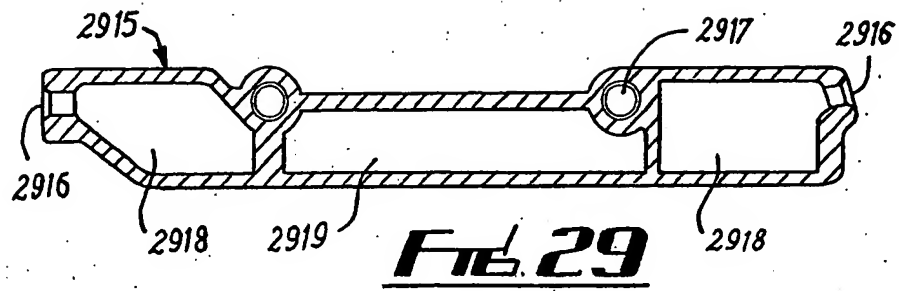


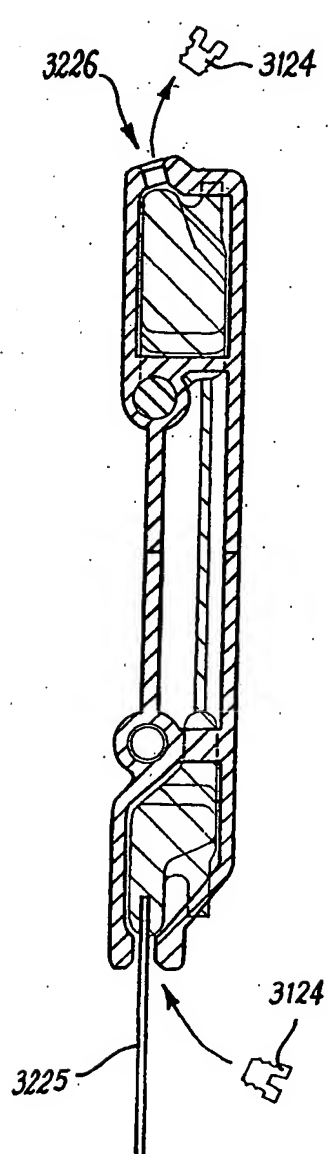
**FIG. 23**



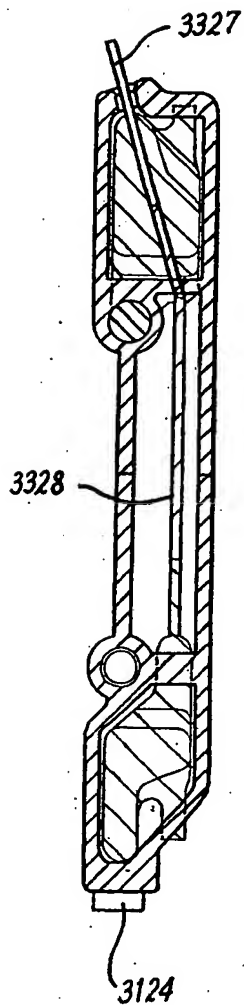
**FIG. 24**



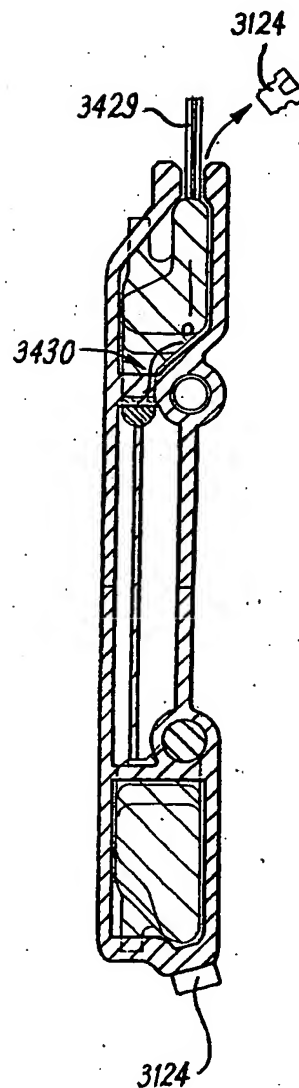




**FIG. 32**

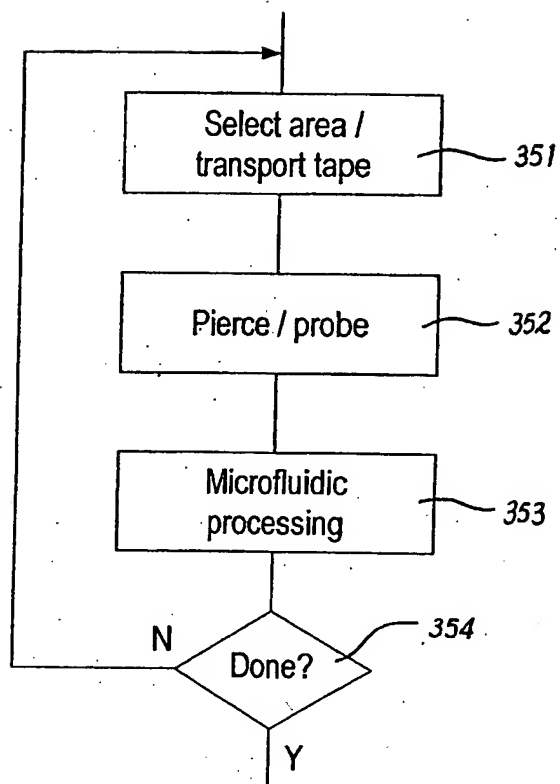


**FIG. 33**



**FIG. 34**





**FIG. 35**